ANNALS
OF
OTOLOGY, RHINOLOGY
AND
LARYNGOLOGY

VOL. 66 SEPTEMBER, 1957 No. 3

XLV

INDIVIDUAL DIFFERENCES IN FUNCTIONAL RECOVERY AND STRUCTURAL REPAIR FOLLOWING OVERSTIMULATION OF THE GUINEA PIG EAR

MERLE LAWRENCE, PH.D.
PHILLIP A. YANTIS, PH.D.
ANN ARBOR, MICH.

It is well established that when permanent damage by acoustic overstimulation of the ear has been created the effects show up as a derangement of the organ of Corti. But in early overstimulation deafness (a loss of sensitivity that has just recently been produced or one that may not have yet stabilized at its full loss or recovery), the audiometric shift in threshold may not reflect entirely alteration within the sensory elements. There are apparently other things that happen in these early stages.

Such events are indicated by the discrepancies revealed in experiments dealing solely with the electrical output of the organ of Corti and those reporting behavioral measures of hearing following overstimulation. The latter give evidence of a fairly specific frequency loss, although not necessarily at the overstimulating frequency, while a more generalized loss appears in the electrical measures. Therefore,

From the Physiological Acoustics Laboratory, Department of Otolaryngology and Institute of Industrial Health, School of Medicine, University of Michigan. This investigation was supported in part by the Research and Development Division, Office of the Surgeon General, Department of the Army, under Contract No. DA-49-007-MD-634.

Presented at the Fifty-Third Meeting of the Acoustical Society of America, New York City, May 23-25, 1957.

when pure-tone audiometry reveals a hearing loss immediately after overstimulation, one cannot say, on the basis of this alone, how much loss is the result of altered function of the organ of Corti and how much is attributable to some change in neural activity.

There are innumerable studies reporting the changes within the organ of Corti following acoustic overstimulation, and Hammer[7] and earlier Hamberger and Hydén,[5] and Hamberger, Hydén and Nilsson[6] have reported some cytochemical changes within the spiral ganglion cells following shock wave stimulation. But a complete knowledge of the temporary and permanent effects of sound, or even of hearing itself, will not be achieved until the effects upon the organ of Corti, the nerve and nerve endings, and their mutual relationship are thoroughly understood. In order to throw a little more light on the nature of stimulation deafness we have sought, in the investigation reported here, to learn more about the pattern of recovery in the organ of Corti.

In these experiments we have not been concerned with correlating areas of damage with loss of response to certain frequencies, nor with any theories of peripheral analysis or sound distribution. We have investigated, in a limited way, the process of recovery and repair following different degrees of initial destruction.

Obviously, the interpretation of results is determined to a considerable extent by the way in which the initial damage is produced, and there are at least three variables other than those concerned with frequency to be considered in this respect. Two are concerned with intensity: the overstimulating sound can be produced at a particular pressure level or it can be adjusted to a level that is a certain amount with respect to the maximum or some other related electrical output of the animal. The first procedure puts all animals in the same environment while the other adjusts the environment so as to have the same effectiveness on each animal, and takes into account the inherent sensitivity of the animal's ear. The third variable is time. In order to produce different degrees of aural destruction an overstimulating sound can be left on for different periods of time.

Our purpose in these experiments has been to study the individual differences in amount of impairment and recovery. Therefore, for each group of animals, the overstimulating sound was kept as much the same for each animal as possible without compensating for sensitivity which is considered an important contributing factor to the individual differences. The duration of exposure remained the

same and the sound pressure level was measured at the outside of the drum membrane. Two levels of overstimulating sound, each on a different group of guinea pigs, were used and we investigated the activity of the organ of Corti as manifest in its electrical response before noise, immediately after, and approximately two months later, after considerable recovery or further loss has taken place. In addition to this, the structure of the organ of Corti, after sacrifice of the animal following the two-month later test, has been examined to determine the nature of repair of this structure in relation to the amount of electrical response recovered or lost.

PROCEDURE

A total of 37 guinea pigs was used in these experiments. Of this number 5 served as controls for the purpose of checking on the possible impairment of function introduced by the surgical procedures. The remaining 32 animals were divided into two groups, each of which was stimulated by a different level of noise. These two groups will be referred to as Series 1 and Series 2.

Each animal was first deeply anesthetized with sodium pentobarbitol and maintained in this state with occasional use of ether. The sodium pentobarbitol was a 50 mg per cc solution given in the dosages of 0.6 cc per kg of body weight for animals weighing less than 500 gms and of 0.8 cc per kg for animals weighing more than 500 gms.

The operative field was shaved, washed thoroughly, and sterilized. The middle ear was then exposed through a small opening in the skin and bone just posterior to the external meatus. A small plastic speculum containing a concentric probe tube was inserted into the external meatus so as to approach the drum membrane as closely as possible. The speculum was connected to a nonmetallic pipe which passed through the wall of the electrically shielded soundproof room in which the experiments were conducted, and then connected to a University PA-30 driver unit which was activated by the sound-producing equipment.

The small concentric probe came out the side of the sound speculum through an air-tight seal and served as the probe of a probe —W. E. 640AA condenser microphone arrangement used for measuring the sound source. Because of the variations of the animals' ears and our inability to reproduce the exact stimulus conditions from animal to animal, determination of sound pressure for all frequencies

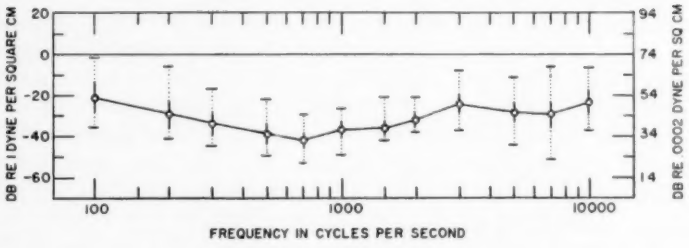

Fig. 1.—Normal 1-microvolt sensitivity curve. Each point is the mean of 35 ears, the ordinate showing the sound pressure necessary to produce 1 microvolt of response at the indicated frequency. The solid vertical line is the standard deviation and the dotted line shows the range.

used was made for each animal every time by means of the probe-microphone system. By using this method all results can be, and are, expressed in terms of the actual sound pressure used.

A small, sterile, platinum foil electrode was placed on the round window membrane and an indifferent electrode inserted into the nearby skin of the animal. These led to a battery-operated amplifier within the shielded room and then to a General Radio type 736-A Wave Analyzer outside the room. The recording system was calibrated so that electrical output from the animal could be read in terms of microvolts at the round window.

In both groups, one ear of each animal was first tested for sensitivity. That is, at each of 12 frequencies, 100, 200, 300, 500, 700, 1000, 1500, 2000, 3000, 5000, 7000 and 10,000 cps, the sound pressure at the tympanic membrane necessary to give a response of one microvolt at the round window was determined.

The same ear of the animal was then subjected to a noise generated by a General Radio type 1390-A Random-Noise Generator. Those animals in Series 1 received an over-all noise level of 150 db above .0002 dyne/cm^2 as measured at the drum membrane. Those in Series 2 received approximately 136 db above the same reference level.

Following 20 minutes of this stimulation there was a short waiting period for the electrical response of the animal to settle down, after which the sound pressure required to produce one microvolt at each of the 12 frequencies in the same ear was again recorded.

The electrodes and sound speculum were then removed, the wound sprinkled with sulfadiazine powder and closed with four or five wound clips. The closed incision was covered with collodion and the animal allowed to recover. Fifty-six days later the previously stimulated ear of each animal was again operated upon and the sensitivity measures recorded for the third time.

While the animal was still deeply anesthetized following this last set of recordings the chest cavity was opened and the head region perfused with warm saline and Maximow's mercuric-dichromate-formaldehyde solution. Both temporal bones were removed and processed for celloidin embedding. By carrying both temporal bones through the histological processing the unstimulated ear of each animal served as a control for the other, stimulated ear of the same animal. Each bone was sectioned at 20 microns, and every fifth section stained in hematoxylin and eosin and mounted in serial order. A careful microscopic study was made of all structures composing the organ of Corti and the scala media from base to apex in both ears of each animal. A graphic reconstruction[4] of each ear was made together with tabulations of all abnormalities in structure. In many instances serial photomicrographs were taken to record various degrees of recovery or degeneration of the structures within the scala media.

CALIBRATION OF SOUND SOURCE AND RECORDING EQUIPMENT

The small sound probe and W. E. 640AA microphone were calibrated so that a known voltage from this system represented a certain sound pressure at the open end of the probe. Since the sound tube and its concentric, calibrated probe were tightly sewn within the external meatus and placed just distal to the tympanic membrane, the sound pressure for each tone presentation could be, and was, determined. This probe tube was also employed in determining the level of noise used to overstimulate the ear and to determine the purity of the stimulus.

Determination of the level of noise used for the two series of animals was carried out in the following way. First, the stimulus-oscillator output voltage and attenuator settings necessary to give 1 dyne/cm^2 at the animal's drum membrane was determined for a pure tone of 1000 cps. The output from the probe-microphone combination for this frequency and sound pressure level was fed to

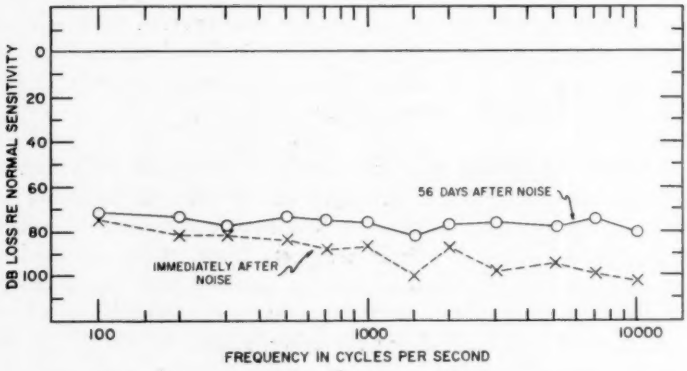

Fig. 2.—Series 1. Mean 1-microvolt sensitivity curves for 15 animals immediately after noise and for 10 of the same animals 56 days later. A frequency for which no response could be obtained was arbitrarily assigned a loss of 120 db for purposes of calculating the mean.

a Daven type 35-A Distortion and Noise Measuring set, and the amount of output was read on the DBM meter. The tone was then turned off. Noise was substituted in the stimulus system and raised in intensity to the amount necessary to give an output at the limit of linearity of the closed-tube speaker system. This was found to be, on the Daven DBM meter, 62 db above the pure-tone 1 dyne/cm^2 level, or 136 db above the customary .0002 dyne/cm.^{2} This noise level at the drum membrane of the animal's ear served as the damaging noise for Series 2. For Series 1 the noise voltage to the speaker was raised 20 db, but the calibrating system showed the actual acoustic noise to raise only 14 db because of the overloading of the speaker. So this 14-db increase, representing 150 db above .0002 dyne/cm^2, was used for the noise stimulus of Series 1. During the 20 minutes of noise stimulation the level was continually monitored by the Daven 35-A. Frequency analysis of the noise by means of the probe and wave analyzer showed a fairly uniform spectrum from 100 to 10,000 cps for the 150-db noise level. There was a gradual increase in intensity with higher frequencies, so that 10,000 cps was about 12 db stronger than 100 cps. For the 136-db noise stimulus the peak intensity appeared around 1000 cps, being about 8 db more intense than at 100 cps, and around 18 db greater than at 10,000 cps. These figures represent the values of the actual acoustic presentation and reflect the properties of the speaker and sound tube.

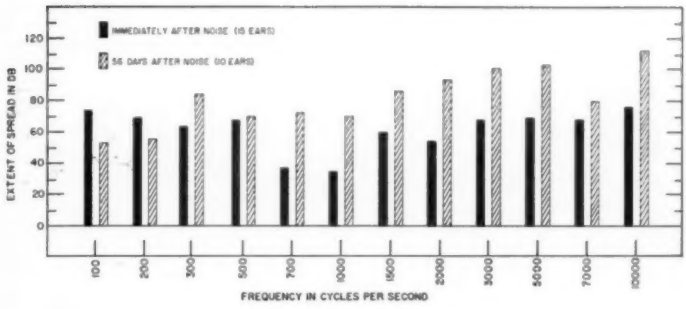

Fig. 3.—Series 1. The range from greatest loss to least loss in sensitivity at each frequency: immediately after noise compared with 56 days later. Lower end of range arbitrarily placed on a zero-decibel line.

The amplifiers recording the potentials arising from the cochlea of the animal produced a known amplification so that readings on the wave-analyzer could be directly interpreted in terms of microvolts at the round-window membrane.

RESULTS

1. FUNCTIONAL RECOVERY

Aside from the five control animals that were not stimulated by noise, two were found on the first test to have a conductive loss caused by dirt in the external meatus, and one animal died while being stimulated with the 150-db level of noise. This latter animal has been included in the normal sensitivity data but, of course, in nothing else. The other two were carried through as a separate group to furnish incidental data on the protective effects of the conductive impairment.

Of the 29 remaining animals, 15 were in Series 1 and 14 were in Series 2. During the 56-days recovery period some animals died, were too infected, or the bone in the operated area had so overgrown that an approach to the round window was impossible. This left 10 animals in Series 1 and 9 in Series 2 for the final measures. All that lived, however, were perfused for histology and the final number of ears examined was twice the number of animals because each unstimulated ear was carried through with the other, stimulated one.

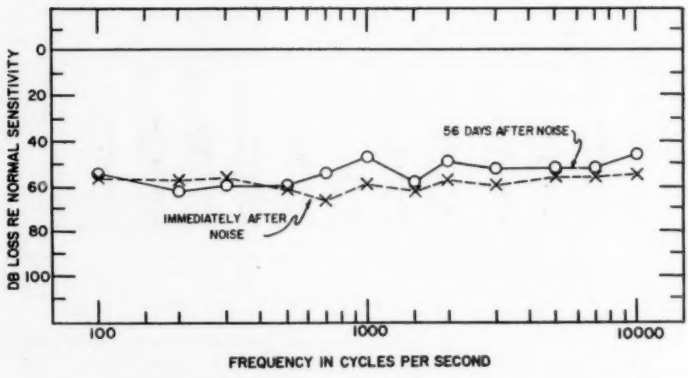

Fig. 4.—Series 2. Mean 1-microvolt sensitivity curves for 14 animals immediately after noise and for 9 of the same animals 5 days later.

Controls. The five animals serving as controls in the general operative and recording procedures were not all done at the same time, but were dispersed throughout the entire series of experiments, the first of which was carried out in October 1954. Sensitivity measures were first made on these animals using the standard technique. The wound was then closed and the animals allowed to recover for the 56-day period. In one there was such an overgrowth of bone that attempts to place the electrode punctured the round window and the animal had to be discarded. There appeared some loss in sensitivity in the average results from these control ears, the greatest being for the low frequencies and the least for the highs with an improvement at 10,000 cps. The average loss in sensitivity for all frequencies was 9.6 db so the experimental results can be interpreted within these limitations.

In order to establish a base line from which sensitivity shifts could be measured, the sound pressure necessary to give a 1-microvolt response for the 12 frequencies was first established on each of the 35 apparently normal ears. Figure 1 shows the average results at each frequency. The solid vertical line about each point shows the standard deviation and the dotted line denotes the range. This curve corresponds remarkably well with other such published curves for the guinea pig,[1] and served in these experiments as a guinea pig threshold curve on the basis of which an animal was judged as possessing normal sensitivity or not. It was on this comparison that the two animals

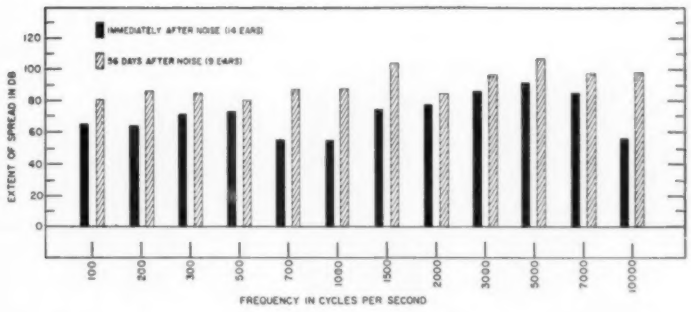

Fig. 5.—Series 2. The range from greatest loss to least loss in sensitivity at each frequency: immediately after noise compared with 5 days later. Lower end of range arbitrarily placed on a zero-decibel line.

were discarded and then found to have dirt impacted in their external canals.

Experimental Animals. The noise level used to overstimulate the animals in Series 1 was such that in many cases there was complete loss of response at some frequencies. In this case an arbitrary loss of 120 db was assigned the frequency so that a mean curve of sensitivity shift immediately after noise could be plotted. This measure has been compared with that after a 56-day recovery period, and is shown in Figure 2. The loss is very uniform and after the 56-day recovery period shows the greatest improvement for the higher frequencies. These two curves represent the means of the groups: 15 ears immediately after noise and 10 of the same ears 56 days later. It shows that despite the severity of loss there is, on the average, a regaining of sensitivity.

Immediately following this extreme amount of noise which produces some degree of loss in every ear, there is, nevertheless, a noticeable degree of variation from animal to animal in the amount of sensitivity shift. There is also, as Figure 1 shows, some variation in the normal sensitivity curves and it is not possible to say with certainty whether or not the same factors which affect initial sensitivity are also determining the degree of loss an animal experiences. That is, the differences in normal sensitivity may reflect the ease with which the sound gets through the middle ear into the inner ear, in which case the most sensitive would be damaged the greatest amount. But

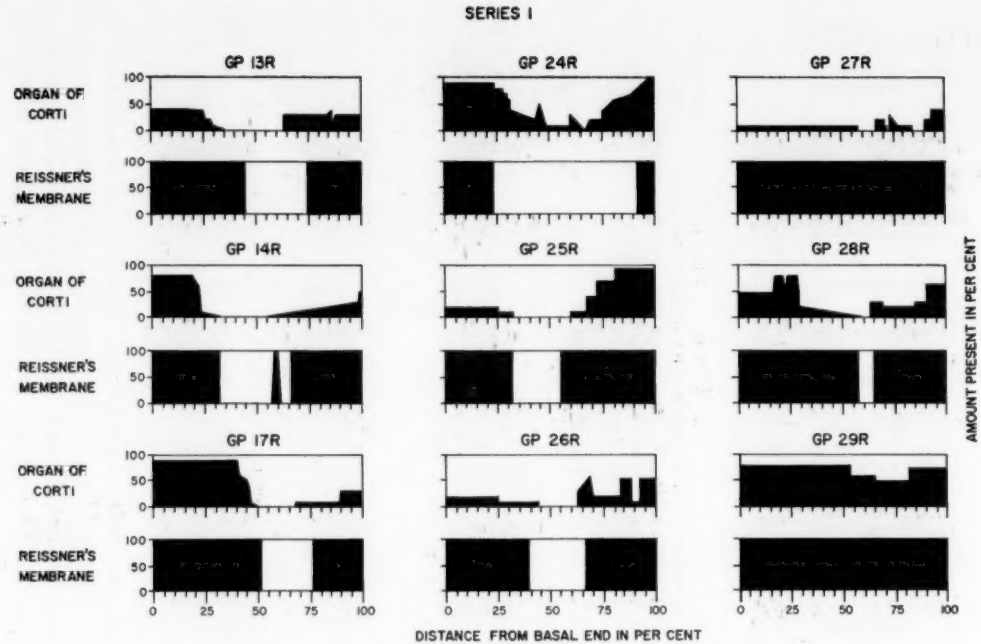

Fig. 6.—Linear plots of the condition of the organ of Corti and Reissner's membrane for the overstimulated ears of Series 1. These plots were taken from individual graphic reconstructions and the distance along the basilar membrane changed from millimeters to per cent so that comparable distances among ears could be determined. Black areas for the organ of Corti show its condition in per cent according to the criteria explained in the text. Black areas for Reissner's membrane indicate it as being intact.

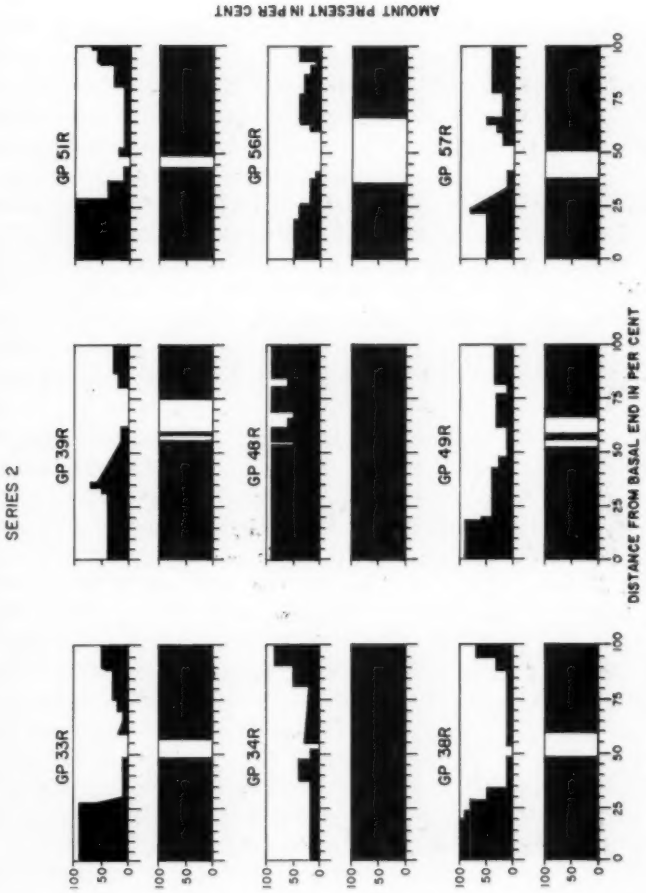

Fig. 7.—Same as Figure 6. Series 2.

the degree of initial loss does not necessarily indicate the amount of further recovery or loss.

An indication of the extent of this can be seen in Figure 3. Here the bars represent the range from greatest loss to least loss: immediately after noise compared with 56 days later. The sensitivity of some animals for some frequencies has improved; in others it has continued to decrease during the 56-day recovery period. To show this, the greatest loss for any animal at that frequency has arbitrarily been placed on a zero-db line. This clearly shows the extensive increase in spread of sensitivities among animals after the 56-day period except for the two lowest frequencies. As will be shown later, the amount of initial loss at any frequency is no indication that an animal will recover function or lose it further at that frequency even though, as shown here, the extent of spread among animals increases. Before discussing this further it is best to look at the results from Series 2.

As explained earlier, the ears of Series 2 were overstimulated by a noise 14-db less intense than that of Series 1. Figure 4 is comparable to Figure 2 for Series 1 and shows the mean loss at each indicated frequency for 14 ears immediately after noise and for 9 of these same ears 56 days later. Here again the loss is remarkably uniform, but about 25 db less than that for Series 1. The mean amount of recovery in this instance is also less, but still shows some tendency for greater improvement at the high frequencies. There is evident again an increase in spread from the animal with the greatest loss in sensitivity to that with the least. Figure 5 shows this spread and can be compared with Figure 3 for Series 1. The initial spread immediately after noise appears to be greater in Series 2 than in Series 1, but this is probably due to the total deafness produced for some frequencies in some animals in Series 1 and the arbitrary cut-off level of 120 db. Despite the increase in spread following the 56-day period there is little shift in the mean shown in Figure 4, which indicates that the amount of loss among the animals is just about equal to the amount of gain. Here again the amount of initial loss does not indicate whether or not an animal will continue to lose sensitivity or regain it during the quiet period after noise, but by comparing the results from Series 1 with Series 2 we can get some idea of this relationship.

If the degree of permanent loss is related to the amount of initial damage it could be expected that more of those animals of a group which show the least loss immediately following a period of overstimulation would show subsequent improvement than would those

that suffered the greater initial damage. In other words, in Series 1, more of those animals which showed the least amount of sensitivity shift following the noise would be expected to show a recovery toward normal sensitivity during a 56-day period than of those which showed the greatest amount of initial sensitivity shift. This situation has been simulated by the conditions of Series 2 in which most animals showed less of an initial sensitivity shift following noise than did those animals of Series 1. Granted, the noise level was less in Series 2 than Series 1, but this does not change the supposition which refers to the condition of the organ of Corti and its function following the overstimulation, regardless of level.

If, then, we compare the percentage of animals in Series 2 that show definite recovery with the percentage of animals of Series 1, we would expect to find a greater percentage recovering in Series 2 than in Series 1. Such is not the case, however. In Series 2, 56 per cent showed recovery, 11 per cent showed no change, and 33 per cent showed a loss. In Series 1, 60 per cent showed recovery, 10 per cent showed no change, and 30 per cent showed a loss. These groups are small but the similarity between groups, considering the marked difference in initial loss following the overstimulation, is significant. It may be, however, that this is a universal figure for guinea pigs and that the essential factor concerns the amount of recovery after one level of overstimulation as compared to another rather than the number of those recovering. If such is the case one would expect there to be a much greater amount of recovery in those ears of Series 2 that show a subsequent gain in sensitivity than those showing subsequent gain in Series 1. We have calculated the average decibel gain for all frequencies of those ears in Series 1 that showed recovery for comparison with the same figure for the recovered ears of Series 2. In Series 1 the average gain in sensitivity is 21 db and in Series 2 it is 22 db. These figures are remarkably similar in view of the great amount of difference in initial loss of the two series. Calculating the average amount lost is not as meaningful since some of the animals in Series 1 were completely insensitive to some tones and could lose no more during the 56-day period. So we would expect to find this figure greater for Series 2. The average loss in sensitivity for those ears that showed no improvement during the 56-day period was 10 db for Series 1 and 19 db for Series 2.

It may be, of course, that this 22-db average gain for both groups merely means that both were recovering at the same rate. It is possible that recovering ears of Series 2 may have done much better

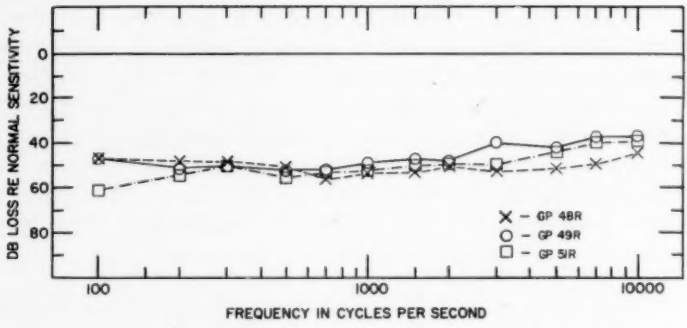

Fig. 8.—The temporary shift in 1-microvolt sensitivity produced in three ears of Series 2. These measurements were made shortly after cessation of the overstimulation.

in the long run than those of Series 1. But from the data here we have no way of knowing this. This 22-db recovery figure also must be considered in the light of the 10-db shift found in the controls associated with the experimental technique.

However, these results do seem to indicate that the degree of sensitivity shift immediately after overstimulation by very loud noise does not indicate which ears will recover or which will continue to lose, nor does this initial shift seem to influence the rate of the recovery process.

This suggests the possibility that, following a period of acoustic overstimulation, the permanent loss of function of the organ of Corti is not determined so much by the amount of initial loss suffered by an individual ear as by its ability to recover. If two ears suffer different degrees of loss following overstimulation by some sound, it is not this initial difference that determines the permanent loss but the ability, in each case, of the sensory elements to recover. This principle we shall refer to again in the discussion of the histological studies on structural repair.

2. STRUCTURAL REPAIR

The original purpose of processing both ears of an experimental animal was to examine the unstimulated, control ear of each animal

to see if an anatomical reason could be found to explain why some ears were damaged more than others. However, except for some slight differences in appearance attributable to small variations in amount of autolysis, no morphological characteristic related to the damage produced in the opposite ear could be found. When the electrical data were examined and the "recovery principle" appeared to be operating rather than an initial predisposition to injury, it seemed clear that the factors present in the ear that determine its ability to recover may be of a nutritional or chemical nature too subtle to see in the routine histologic examination of a normal ear.

Both ears of all the animals in Series 1 (total of 20) and all those in Series 2 (total of 18), plus both ears of the controls, and those with bony overgrowth following the 56-day period, were examined and graphically reconstructed. A complete total of 60 ears was studied.

Since a careful study of the control ear on each animal revealed nothing to account for the degree of loss or lack of loss following overstimulation in the opposite ear it was decided that whatever was determining the ability to recover could not be found in the normal ear with the techniques being used and that the damaged ear itself should be examined.

The first step was to convert the spiral graphic data into linear charts with the length of the basilar membrane converted into per cent, rather than millimeters, so that similar points in the different ears could be compared directly. It was noticed that in almost every case Reissner's membrane was ruptured and it seemed quite probable that this might have a significant influence on the eventual repair. So the tears in Reissner's membrane were plotted along with the structures of the organ of Corti.

The criteria for judging the state of repair of the organ of Corti was necessarily an arbitrary one, but since it was not known what structures might be important for the general repair of damaged areas, a rather extensive scale in per cent was used to express the amount of total structure present. The scale was as follows: 0 per cent—bare basilar membrane; 10 per cent—single layer of cells on basilar membrane; 20 per cent—layer of cells and small mound where arch would be; 30 per cent—layer of cells and large mound; 40 per cent—mound with visible arch present; 50 per cent—arch with one hair cell present; 60 per cent—arch with two hair cells present; 70 per cent—arch with three hair cells present; 80 per cent—arch with

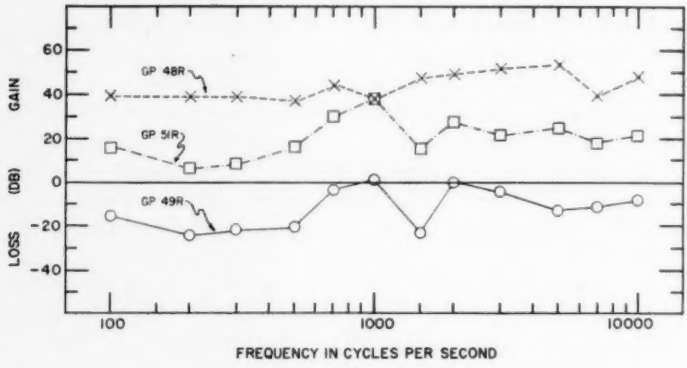

Fig. 9.—The amount of sensitivity gained or lost by the same three ears of Series 2 shown in Figure 8 during the 56-day period following overstimulation. The initial loss immediately following the noise gave no indication of the subsequent sensitivity of these ears.

four hair cells and distinct Deiters' cells; and 100 per cent—normal, clear-cut organ of Corti.

Other structures were examined and their condition noted on the spiral reconstruction, but this information was not recorded on the linear graph. These structures included the Claudius cells, external sulcus cells, spiral ligament, spiral prominence, stria vascularis, and internal sulcus.

By referring to the spiral graphic reconstruction the condition of the organ of Corti in accordance with the above scale was determined for every 100 microns, which was the distance between the cut sections. This percentage figure was transferred to the linear graph.

Figure 6 shows linear reconstructions for the ears of Series 1 and Figure 7 for the ears of Series 2. There are only 9 graphs shown in Series 1 because in one ear the cochlea was mechanically damaged during removal of the recording electrode and it is not clear whether the histologic picture reflects this damage or that caused by the noise.

The most noticeable thing about these graphs is the lack of uniformity in the areas or patterns of destruction. The most severe

destruction appears generally around the 50 per cent point and in most instances Reissner's membrane is also reptured in this region. The extent of these areas as well as the transition regions can only be demonstrated by the method of graphic reconstruction.

The appearance of the organ of Corti after acoustic destruction has often been described, as well as the fact that Reissner's membrane may be ruptured upon strong enough stimulation. The chemical constitution of the fluids on the two sides of this membrane is quite different in electrolyte content,[13] and any contamination of the endolymph by perilymph has a deleterious effect upon the organ of Corti. As has been indicated by Eldredge, Covell and Davis,[3] when this membrane is ruptured there appears to be more extensive damage of the organ of Corti toward the apex than toward the base. The opposite effect is seen in cases of inner-ear destruction through other means such as hypoxia.[12] In general apical damage is found in the ears reported here, but there are exceptions: in Series 1, ear 25R, and in Series 2, ear 34R, have the most serious destruction in the basal region.

As mentioned earlier, examining an ear histologically a certain period of time after the ear has been subjected to a damaging level of sound does not give a definite picture of what has transpired in that ear because, without functional measures, it is not possible to tell whether the particular ear being examined has undergone repair or further degeneration.

Earlier we mentioned the apparent importance of the ears' ability to recover and our inability to find any structural deviation in the control ears of each animal that might be related to this ability, assuming that both ears of the same animal would act alike. To illustrate this, Figure 8 shows the 1-microvolt sensitivity curves from three animals of Series 2 immediately after the 20 minutes of 136 db noise and Figure 9 shows the amount of further gain or loss during the subsequent 56-day period. The ear of guinea pig 48 recovered 40 db, almost returning to normal, while 51R recovered only 20 db on the average, and 49R remained the same at some frequencies or lost at others.

Closer examination of the serial sections of these ears does, however, disclose two histological changes that may very well be related to the extent of structural repair which the organ of Corti may undergo.

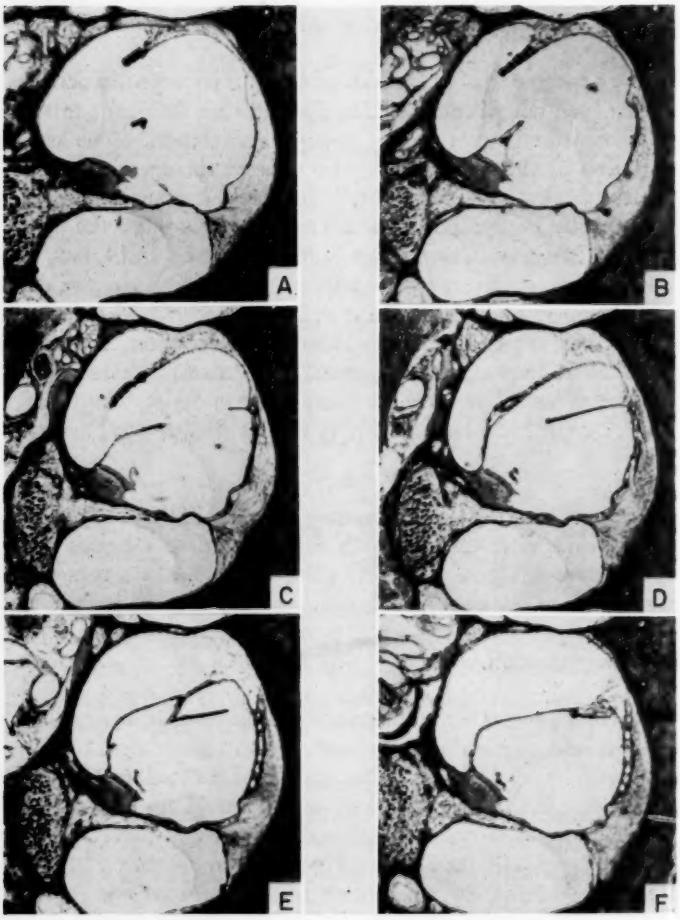

Fig. 10.—Photomicrographs of serial sections of guinea pig 51R to show the regeneration of a Reissner's membrane. Sensitivity curves for this ear are shown in Figures 8 and 9, and the graphic reconstruction is shown in Figure 7. This region of regeneration is occurring at the point along the basilar membrane which is 50 per cent between base and apex.

One is that Reissner's membrane can repair itself if the break is not too great, and even then there are indications that, given time, it might. The other is that certain cells of the external sulcus persist after all else in the scala media has been destroyed.

In the above mentioned study by Eldredge, Covell and Davis, the authors state that the torn edges of Reissner's membrane may take on a club-like shape. When serial sections are studied it is often seen that these are part of a repair process which the membrane is undergoing. This attempted repair is seen in most of the ears and the following is a typical example.

Figure 10 is a series of photomicrographs taken at the edge of the tear in the overstimulated ear of animal 51. The linear graphic reconstruction is shown as part of Series 2 in Figure 7 and the photomicrographs are taken in the region of the 50 per cent point between the base and apex as indicated.

In (a) of Figure 10 (ear 51R of Series 2) the remnants of Reissner's membrane can be seen in the middle of the now combined scala vestibuli and scala media. The organ of Corti is completely missing. The stria vascularis has degenerated, and the connective tissue cells of the spiral ligament are no longer visible except in the region of the scala tympani. This latter observation is very interesting in that it would appear that survival of these cells is somehow related to the intact scala tympani. A protrusion of scar tissue can be seen at the top bony border between turns of the cochlea. In picture (b), which is 5 sections or 0.1 mm further toward the apex in this same turn, the continued extensive degeneration and a larger piece of the remaining Reissner's membrane can be seen. The connective tissue scar has extended a little further down toward the limbus. In (c), part of the original Reissner's membrane is shown. This section is another 0.1 mm toward the apex around the same turn and, as shown in the reconstructions of Figure 10, is at the edge of the tear. One can visualize that the membrane would have a jagged appearance if the edge of the disruption could be viewed from above, and this section has caught an area where a bit is still attached at its two ends. In the normal position, Reissner's membrane extends from the upper margin of the stria vascularis to the medial edge of the spiral limbus as shown in this section. The regenerating connective tissue always starts from a region above the stria vascularis extending from the membrane lining the bony partition between turns, as shown here. In picture (d), another 0.1 mm apicalward, the new Reissner's membrane is

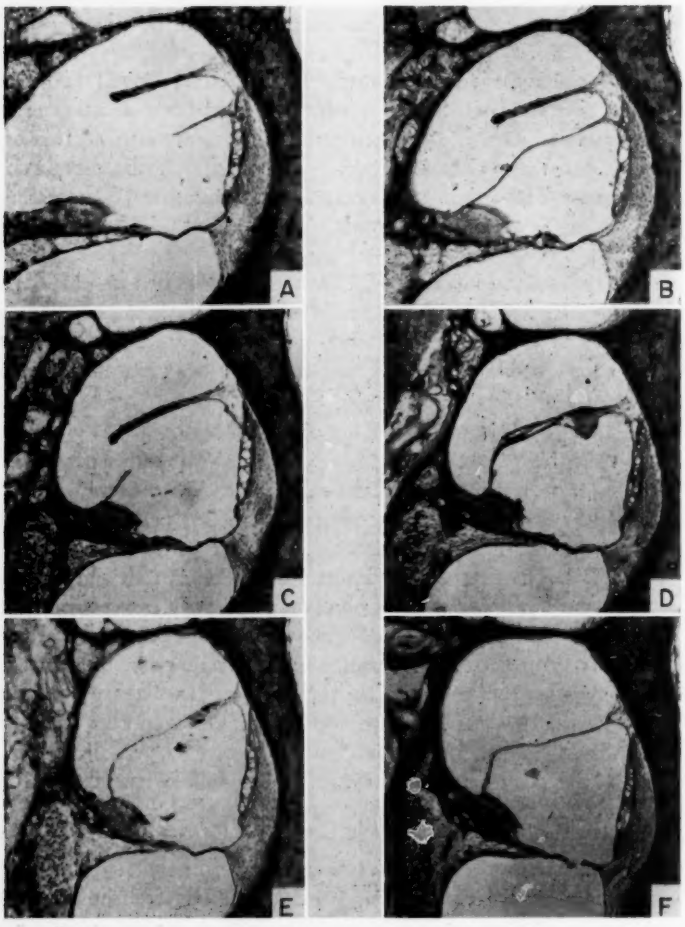

Fig. 11.—Photomicrographs of serial sections of guinea pig 57R to show the regeneration of Reissner's membrane. The graphic reconstruction for this ear can be seen in Figure 7. This regeneration is occurring at the point 50 per cent up from the basal end and shows that a regenerated membrane can thin down to appear like a normal one except for its attachment high up on the spiral ligament above the stria vascularis.

complete and parts of the old torn one can be seen. The basilar membrane now has a layer of cells and the stria vascularis, though extensively vacuolated, is in considerably better condition than that of picture (a). The connective tissue cells of the spiral ligament also are now visible. As we proceed toward the apex another 0.1 mm to picture (e), the regenerated Reissner's membrane has begun to thin down and either joins up with the untorn remainder of the old membrane or, in this region, has taken on the appearance of a normal one. Picture (f) shows an almost normal membrane. The nerve fibers in the spiral osseous lamina appear more numerous than in picture (a) but otherwise the organ of Corti is still completely gone. The appearance of a layer of cells together with a small mound on the basilar membrane of picture (c), (d) and (e) are shown in the graphic reconstruction of this ear in Figure 7 as an increase of structures to about 20 per cent, as outlined earlier, and appear just at the 50 per cent point of the basilar membrane proceeding from base to apex. This provides an orientation region for comparing the photomicrographs of Figure 10 with the reconstruction of Figure 7.

There is, of course, no way in which a Reissner's membrane that appears normal 56 days after a drastic acoustic insult can be recognized as having remained normal or as having regenerated. That the newly formed membrane that appears as thickened connective tissue in the region of the break can thin down to a normal appearance is indicated by the fact that a normal-appearing membrane appears at the edge of a break but attached much too high up above the spiral ligament to be a normal membrane. The regeneration of a new Reissner's membrane in ear 57R of Series 2 is shown in Figure 11 to illustrate this point. The photomicrographs portray sections of a turn of the cochlea proceeding by 0.1-mm steps from near the midpoint of the basilar membrane toward the apex. The reconstruction of Figure 7 shows the region of the denuded basilar membrane and the tear in Reissner's membrane for this ear. Pictures (a), (b), (c) and (d) show the newly formed scar which finally closes the gap between scala vestibuli and scala media. In (d) the membrane is thick and vascular, but as we proceed toward the apex by two more 0.1-mm steps we see that the scar thins out until, in picture (f), it is as thin as a normal Reissner's membrane but is attached way above the normal point of attachment at the top of the stria vascularis. This indicates quite clearly that this thin partition between the two scalae is a regenerated membrane. The break is the basilar membrane at this point may be an artifact of the histologic processing and has not been considered part of the picture resulting from the overstimulation.

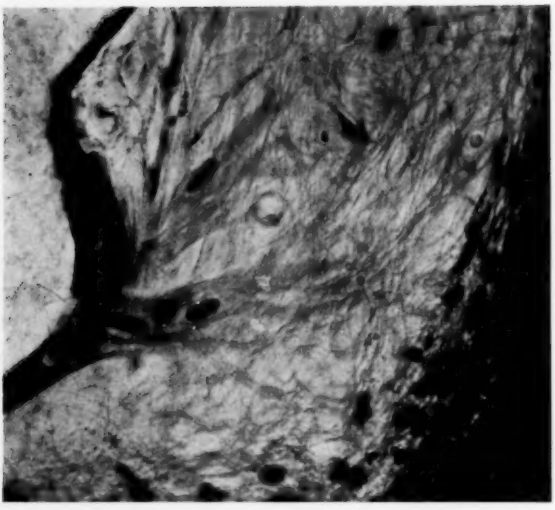

Fig. 12.—External sulcus region of guinea pig 51R. This is a high-power photomicrograph of the section shown in (a) of Figure 10. Those "root-cells" are the only structures to survive, except for the spiral limbus, in this region following overstimulation.

This regeneration occurs at both the apical and basal margin of the tear and there will have to be considerably more investigation before we know the exact relation between this process and the functional state of the organ of Corti.

No evidence of any break in Reissner's membrane could be found for ear 48R of Series 2 or for 29R of Series 1, and in both of these considerable functional recovery occurred. It is also evident from the reconstructions that the organ of Corti in both instances was in fairly good condition after the 56-day recovery period. Since in both instances there was about a 40-db functional recovery for all frequencies, one wonders what these structures looked like immediately after stimulation. It is noteworthy, however, that in these two instances no evidence of the occurrence of any rupture of Reissner's membrane could be found.

With the strong suggestion that an intact Reissner's membrane is essential to any marked functional recovery of the organ of Corti, the two ears that showed intact membranes but considerable degenera-

tion of the organ of Corti were reexamined. These two ears were 27R of Series 1 and 34R of Series 2, and have been plotted in Figure 6 and 7 as having no breaks in Reissner's membrane. On this careful reexamination, however, the membranes of both ears were found to have had, at some time during the 56-day period, a definite break in the membrane.

In 27R, at the 50 per cent point of the basilar membrane, there was found a region where the membrane was attached high up on the spiral ligament much as is shown for ear 57R in Figure 9 (f). There was also a thickened patch in the middle of the membrane in this region that appeared to be a closure by scar tissue rather than normal membrane.

The same situation existed in ear 34R a little above the 50 per cent point of the basilar membrane. In this case, however, a small remaining perforation just below the 55 per cent point had been missed when the graphic reconstruction was made because this gap was filled with a thin fibrin sheet continuous with the rest of the membrane. It is at this point that the organ of Corti is completely gone, leaving a bare basilar membrane.

One other region that has been suggested elsewhere[8] as related to the process of nutrition for the organ of Corti is the external sulcus. This and special cells which we have referred to as "rosette cells" within the spiral prominence appear to be intimately related to the organ of Corti through a direct mechanical connection by means of the fibers of the basilar membrane. There are also within this region cells which extend from the external sulcus either up into the spiral prominence or back into the spiral ligament and which we have called "root-cells" after Boettcher.[2]

After severe overstimulation and a recovery period, all structures of the scala media, including in some cases the connective tissue cells of the spiral ligament above the attachment of the basilar membrane, except for the "root-cells," are degenerated. This is most evident in photomicrograph (a) of Figure 10. Figure 12 is a higher-power picture of the area of the external sulcus showing the nuclei and bodies of these cells in the midst of complete degeneration of all other cells except for those related to the scala tympani.

COMMENT

In this study we have examined the amount of functional recovery as measured by the cochlear potential method and the final struc-

tural picture of ears that suffered two different degrees of initial overstimulation. We have tried to find histological correlates for the degree of recovery by damaging one ear of anesthetized animals of two groups, each group with a different level of intense noise, then sacrificing all the animals after an equal lapse of time (2 months) following the overstimulation. Other investigators have reported attempts to get at this problem of structural repair by overstimulating a large group of animals and then sacrificing them after the lapse of various lengths of time following the trauma.

The most recent of reports using this second method is the one mentioned earlier by Eldredge, Covell and Davis.[3] They exposed a number of animals to tones at a sound pressure level somewhere "between 136 db and 156 db." Small groups were then sacrificed after one, two, seven or 14 days and histological examinations were subsequently made. But, as our study has shown, during a period after overstimulation, about 60 per cent of the ears will undergo an actual recovery, 10 per cent will not change and 30 per cent will experience continued deterioration. Examination of a group of ears at a certain time after stimulation cannot reveal a consistent picture because different things are happening in different individual ears.

The individual differences seem to be related primarily to an ability of the structures of the ear to recover from the insult. The greater the initial exposure, the greater the loss, in general, but some animals' ears may show a greater loss than others. This is the first stage of the individual differences, but this amount of initial loss in any ear does not indicate whether the ear will recover or lose (see again Figures 8 and 9). There is superimposed the possession of an ability, or the lack of an ability, to recover.

It appears further that this recovery, in those ears in which recovery takes place, proceeds at the same rate regardless of the degree of initial loss following the trauma. This has bearing on studies which try to relate, as a psychophysical measure, rate of recovery of normal threshold following the fatigue pursuant to a period of overstimulation in the human ear. In another report[11] we have demonstrated by psychophysical methods what has been known and demonstrated by the cochlear response method for some time, that threshold shifts produced by low level sounds are not the result of changes in the organ of Corti. Only when the sound level is quite high (or possibly left on for long periods of time) does the organ of Corti, the seat of traumatic injury, show a change in sensitivity, and now we see

that average rate of recovery may be the same following two different levels of sound, providing they are of sufficient intensity to alter the performance of the organ of Corti.

It would appear that a most important determinant of whether or not permanent hearing loss will result from an initial threshold shift following intense noise stimulation is the physiological condition of the organ of Corti at the time of insult. A technique for making such a determination has been suggested[9] and has subsequently proven of considerable clinical value in assessing so-called cochlear reserve.[10] All indications are that the same measure should predict the ability of the ear to recover from an acoustic overstimulation.

The actual nature of structural repair following overstimulation may be a very subtle one, related to nutritional and biochemical processes that are not revealed by microscopic examination. One thing is obvious, though, and this is related again to the individual differences and the great intraindividual variations in the status of the inner ear following a recovery period: The full extent of this repair can only be revealed by complete studies of serially mounted sections.

Study reveals that Reissner's membrane can repair itself. It can do this completely if the rupture is not too extensive and it is possible that extensive tears might repair with sufficient passage of time. It is true that the organ of Corti may have suffered irreparable damage by the same vibrations that damaged Reissner's membrane, but up to a point it seems able to undergo some repair itself. The only structures that remain viable after drastic trauma are the cells of the external sulcus. This suggests that we might look more carefully at this area and its relation to the structures of the scala media for the key to the health of the organ of Corti.

SUMMARY

1. Two series of guinea pigs were each stimulated by a different level of high intensity noise (150 db and 136 db at the drum membrane). Each animal was examined by the cochlear potential method for sensitivity before, immediately after and again after a 56-day recovery period. Following this last sensitivity determination the animals were sacrificed by intra-vital perfusion and the temporal bones

removed for histologic processing. One ear of each animal was used for the experimental and histologic procedures; the other served as a normal and control for the histologic processing. Each temporal bone was sectioned at 20 microns, stained in H and E and mounted serially. A graphic reconstruction of each ear was made for the purpose of correlating structural changes with functional activity of the ear at the time of sacrifice.

2. The higher level sound, more intense by 14 db, produced on the average a 25-db greater initial loss in sensitivity than did the lower level sound.

3. When sensitivity measures were made again on each animal 56 days after overstimulation, both groups showed that about 60 per cent regained sensitivity, 10 per cent remained the same and a further loss in sensitivity to normal sounds was present in 30 per cent.

4. The amount of initial loss does not seem to influence the rate at which the ear recovers. In both series the 60 per cent that gained sensitivity during the 56-day recovery period gained a little over 20 db. In Series 2 (those animals that received the lesser overstimulating sound), the 30 per cent that lost sensitivity lost more (19 db) than did the comparable 30 per cent of Series 1 (10 db). This is because many of the ears of Series 1 were completely destroyed and could lose no more.

5. On the basis of the above observations it appears that the eventual permanent loss of sensitivity found in an ear is determined more by its ability to recover than by its initial loss, although the recovery or loss process has to start from the point of initial loss and necessarily reflects it. The degree of initial loss does not, however, indicate whether an ear will recover function or continue to lose it.

6. This (5) explains, no doubt, why no structural weakness or alteration in the control ear of each animal could be found on histologic examination to explain the functional or histological picture in the other, experimental ear. Something more subtle had to be looked for, something related to the nutritional and metabolic process of the scala media. Two structural phenomena were found that still do not explain the ability to recover, but may be related to this process and serve as possible starting points for further investigations:

a) Reissner's membrane has the ability to repair itself.

b) After all else within the scala media has been destroyed by loud sounds and subsequent deterioration, the cells of the external sulcus persist in an apparently viable state.

We are indebted to our assistant, Miss Maxine Clapper, for her skill and careful preparation of the histologic material.

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XLVI

THE ANALYSIS OF VASCULAR REACTIONS IN THE NASAL MUCOSA WITH THE PHOTOELECTRIC PLETHYSMOGRAPH

DARRELL L. DAVIS, PH.D.

AND

ALRICK B. HERTZMAN, PH.D.

ST. LOUIS, MO.

The anatomical descriptions by Swindle[1] of the vascular arrangements in the nasal mucosa indicate that the rates of arterial perfusion of this tissue and the degree of hyperemia could vary independently of each other. Physiological measurements should quantitate both blood flow and blood content in order to complete descriptions of the vascular events and compare their intensities in various subjects under various circumstances. Partial but valuable information is available in direct inspection of the nasal mucosa,[2] in temperature readings[3] and in conventional plethysmograms recorded from the nose.[4,5] Calculations of local thermal conductances from the rates of respiratory heat loss indicate high rates of thermal conductance, i.e., of local blood flow. The extraordinary dimensions of the venous plexus in the nasal mucosa could permit large changes in venous blood content. Such changes have been inferred from visual observations.[2] However, the quantitative relations which may obtain in various circumstances between arterial and venous responses apparently have not been studied in the nasal mucosa.

Earlier studies in this laboratory with the photoelectric plethysmograph[6,7] employed this instrument for purely qualitative observations on the nasal septum. Later success in the quantitation of photoelectric plethysmograms recorded from the finger pad[8] suggested a

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From the Department of Physiology, St. Louis University School of Medicine, St. Louis, Mo.

This work was supported in part by Contract AF 18(600)-1043 between St. Louis University and the Air Research and Development Command with the Arctic Aeromedical Laboratory as the monitoring agency, and in part by Grant H-1804 from the Public Health Service.

re-study of the application of this technique to the nasal septum with the objective of distinguishing variations in the rate of arterial perfusion and in the degree of hyperemia. The correlation which exists between the amplitude of the volume pulse and the rate of arterial perfusion is probably inexact at extremely low or extremely high rates of flow but nevertheless most useful in following continuously a vasomotor reaction. Both our published[8] and unpublished calibrations of the photoelectrically recorded volume pulse in terms of the equivalent change in blood content have demonstrated a fair accuracy of the photoelectric plethysmogram as a record of changes in blood content of the illuminated tissue.

DESCRIPTION OF APPARATUS

The photoelectric plethysmograph as applied to the nasal septum was modified in certain mechanical features from the basic design described in an earlier report.[6] The arrangement is schematically illustrated in Figure 1 and photographically illustrated in Figures 2, 3 and 4. Illumination was provided by an ophthalmoscope bulb capped by a small condensing lens in order to direct a brilliant beam on to the front-surfaced mirror of the periscope tube in which the bulb assembly was mounted. Both periscope tubes were fabricated from stainless steel tubing which was highly polished with jeweler's rouge. The small tube which is seen to extend at a right angle to the long axis of the main tube was added in order to exclude much of the general illumination of the nasal cavity which results from a general scattering of the light emitted from the ophthalmoscope bulb despite its placement within its periscope tube. By careful alignment of the two periscope tubes, the principal photometric effects on the phototube are derived from the tissue lying directly between the two mirrors. Both periscope tubes were so mounted that rotary adjustment in three planes could be effected readily. Firm locking of each tube in any desired position was obtained by the insertion of a compression sleeve between the tube and the locking screw; scoring of the tube by the latter was thus prevented.

Prolonged observations required that this arrangement be mounted on a rigid support which would remain aligned accurately with the particular segment of the nasal septum under observation despite movements of the subject and the considerable mass of the arrangement and which would still not interfere essentially with the comfort of the subject. The previously used mount[6] did not meet these requirements adequately. The arrangement finally adopted and

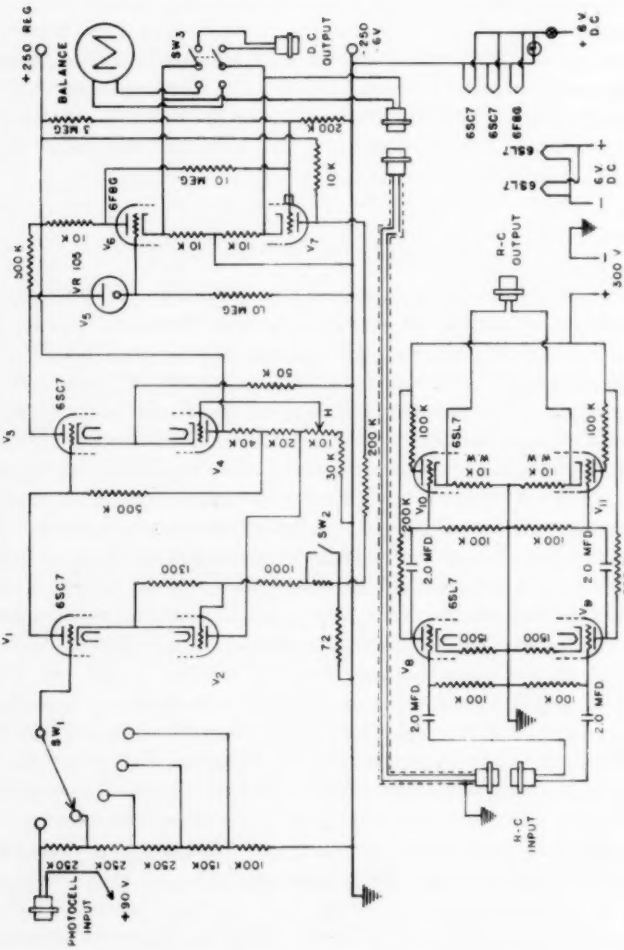

Fig. 5.—Miller DC amplifier and the following condenser coupled amplifier.

partially illustrated in Figure 2 provided for the support of the weight from a helmet (constructed from plaster of paris bandages for each subject) and firm anchoring to the upper denture of the subject. The teeth did not support the weight but served to maintain alignment with the nasal septum. Anchoring to the upper denture was done by fashioning a mouth piece from a dental impression tray filled with impression wax. The tray was in turn attached to the helmet and the mount of the periscope tubes. Flexibility in adjustment was provided by the ball and socket joints shown in the figures. Both mouth pieces and helmets were formed to fit the individual subject. The mouth pieces were stored in 0.1 per cent zephiran solution and the same impressions were used repeatedly on the same subject for several months. Saliva was removed by a dental saliva ejector. The mechanical effectiveness of this mount was demonstrated in prolonged recordings which were free from artifacts and in the simultaneous comfort of the subject.

Photokymographic recording of the variations in the phototube currents was arranged through the use of a D-C amplifier consisting of a slightly modified Miller circuit[8] to which was added a condenser coupled fourth stage. This arrangement permitted simultaneous recordings of the "plethysmographic" trace and of the "volume pulse" trace at different sensitivities. Figures 9 and 10 provide illustrative records in which the trace labelled plethysmogram represents the change in blood content and the trace labelled volume pulse represents only the latter as the slower plethysmographic variations cannot affect this trace due to the short time constant of the condenser coupling.

Circuit details are given in Figure 5. Negative feedback in the amount given stabilizes the amplifier and still allows adequate gain. Output from the third stage may be led simultaneously to a recording galvanometer and to the condenser coupled amplifier for recording of the pulses at exaggerated amplitude. Condenser and grid resistance values in the latter amplifier allow a long enough time constant to permit accurate recording of the pulse amplitude. However, if wave form analysis is required, doubling of either the condenser or the grid leak values lengthens the time constant enough for this purpose. The Miller circuit may be used as a pre-amplifier when a direct writer is preferred for recording the plethysmographic trace and similarly a higher current tube may be substituted for the 6SL7 to drive a direct writer. These modifications do not affect the following discussion. The Miller circuit has been used in this laboratory for about ten years. With stable power supplies, manganin resistors and aged

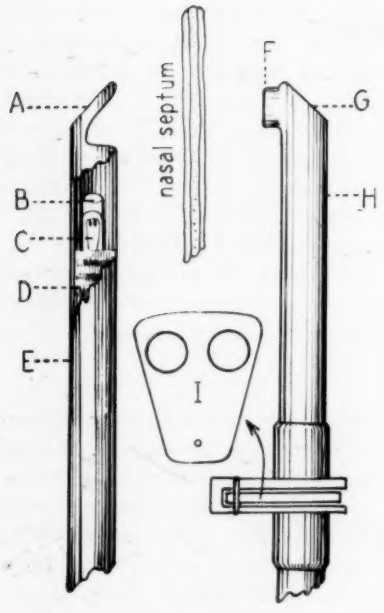

Fig. 1.—Schema of the nasal photoelectric plethysmograph. E and H - periscope tubes of stainless steel tubing; A and G - chromium plated mirrors; C - ophthalmoscope bulb; B - condensing lens; F - small tube which limits extent of the vascular bed influencing the photometry; I - mount for the glass filter which is inserted in one of the holes, the other being empty.

tubes and during operation in a constant temperature laboratory, drift in this amplifier is relatively negligible during an experimental run of eight to ten hours. Although comparable performance is available in commercially available amplifiers, the Miller circuit as used here has certain advantages which are indicated below.

Continuous recordings over prolonged periods of time (three to eight hours) may exhibit drift due to progressive decrease in the emission of the light bulb when the latter is operated on a battery. Substitution of a slightly modified Hartley oscillator with output at 10KC largely eliminates this source of drift with the additional

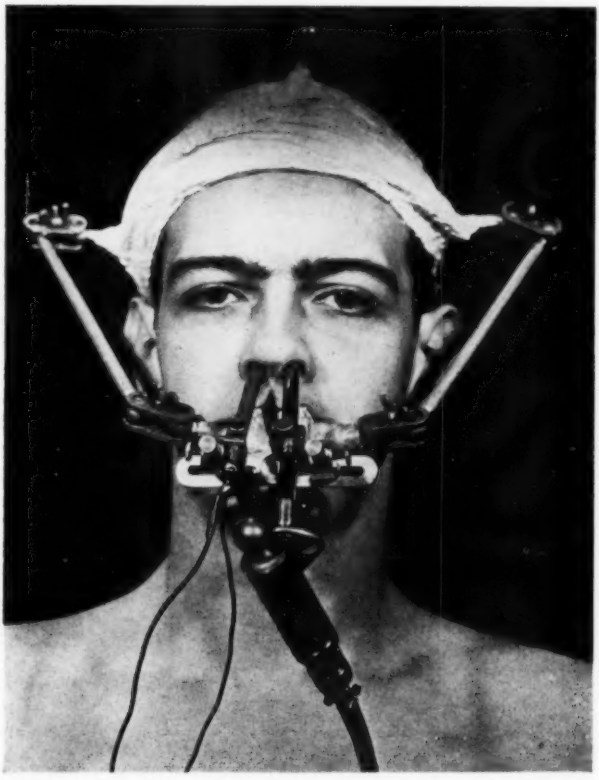

Fig. 2.—Photoelectric plethysmograph for the nasal septum. Note that the weight of the apparatus is carried by rods which are attached to the helmet which has been prepared from plaster paris bandages.

advantage that the oscillator output may be regulated closely by a photoelectric cell directly monitoring the light bulb. Circuit details of the oscillator are given in Figure 6. Several of the values in this circuit are critical for the particular application: C2 should be very nearly equal to 0.002 mfd; $C_1 = 0.5$ mfd when the light bulb requires about 0.55 watt (in many of the designs of the photoelectric plethysmograph illumination is provided by a GE No. 222 bulb—2.2V and 0.25A); R_2 is a ten turn Helipot (5K) which controls the output of the oscillator and allows for very fine regulation of filament voltage. The inductance, L_2, consists of 50 turns of cotton covered wire (No.

Fig. 3.—Side view of the nasal photoelectric plethysmograph.

22) on a spool of plexiglass which is tightly coupled with L_1. When this oscillator is supplied with a well regulated power source, the output is sufficiently constant that only occasional inspection of the light monitor's output is required. This permits infrequent manual adjustment of R_2.

It is preferable to monitor the light emission with a photovoltaic instead of a photoconductive type of light sensitive cell, for two reasons: First, the latter type of sensing unit requires a driving voltage which may change; second, the solid photoconductors have appreciable time constants which prevent accurate registration of rapidly varying light intensity. Therefore, manual adjustment of R_2 in the oscillator circuit may become a "hunting reaction."

The level of the phototube current as generated in the apparatus of Figure 2 may be measured by inserting a sensitive galvanometer or vacuum tube microammeter in the phototube circuit or by using the Miller amplifier in the following manner: The input grid is connected to ground, the circuit balanced by control H (a helipot), and the position of the sliding contact read on the duodial. The grid is connected by means of the attenuator switch to the phototube circuit, the amplifier rebalanced by control H and the duodial read again. Example: in the calibration of a particular amplifier, the duodial readings were 3.55 and 1.88 when grid potential was 0.0V and 0.1V respectively. Although such values remain quite constant during a day's run, it is best to check the zero position each day. The slope of the relation of control H to the input signal at the grid remains quite constant over long periods of time despite small changes in zero position. The initial calibration of the amplifier's balancing control may be done either with known voltages on the input grid or with known input currents in the grid resistor. A convenient level of phototube current is 0.05 microamperes.

Relative gain in the recording traces from the Miller circuit and the CC amplifier may be estimated at any moment by opening the shunting switch, SW_2, in Figure 5. This results in a small increase (one ohm) in cathode resistance and a corresponding shift in the amplifier balance. When the sensitivity of the Miller recording galvanometer is adjusted to meet specific requirements, it is well to keep in mind that this may change the voltage swing at the output cathodes, and thus alter the signal to the CC amplifier. It is useful to arrange for a series-shunting resistance which permits varying the current delivered to the Miller galvanometer without change in the total current drain from the cathodes.

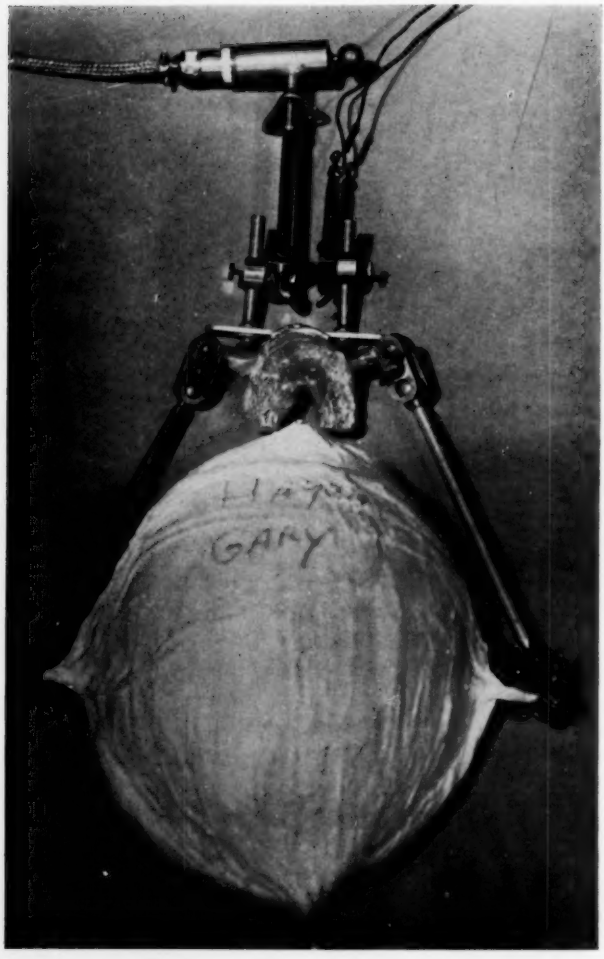

Fig. 4.—View of nasal photoelectric plethysmograph showing relations of the parts and the details of the anchor to the upper denture.

ANALYSIS OF PHOTOELECTRIC PLETHYSMOGRAMS OF THE NASAL SEPTUM

The photometric recordings which we call photoelectric plethysmograms result from variations in the blood content of the transilluminated tissue. The pulsations (called volume pulses) in these traces similarly represent the pulsatile variation in the engorgement of the vessels by the flow pulse. Earlier studies on the fingers[8] demonstrated that the amplitude of the volume pulses correlated with the rate of blood flow and therefore serve as a convenient index of variations in arteriomotor tone.

Two essentially equivalent procedures are available for the quantitation of the photometric records in such terms as to permit comparisons of the relative effects of various procedures on the same vascular bed or, with certain reservations, on different vascular beds. Reference to Figures 7 and 9 will expedite the discussion of these procedures. One of them utilizes the "filter unit" in essentially the same manner as described elsewhere.[8]

In Figure 7, the decrement (A-B) in the photoelectric current due to an undetermined amount of blood in the tissue is unknown. The increment (C-B) in the current due to vasoconstriction is compared with the decrement (F) due to the insertion of the filter. Since F is a constant fraction (.085) rather than an absolute amount, it may matter whether the filter is inserted at B or C. If B is considered to be the "control" level, the filter should be inserted at B if subsequent changes due to variations in blood content are to be referred to the level B; likewise if C is considered to be the control level.

Essentially, this procedure is a matter of comparing fractions, rather than the actual changes in photoelectric current. Hence, one may also measure the latter at B or C and calibrate the kymograms accordingly in terms of per cent change. Choice between the filter calibration or the measurement of the photoelectric current is a matter of experimental convenience rather than basic difference in procedure. The measurements in Figure 9 illustrate the numerical results of calibration.

There may be occasions when the manual manipulation of the filter mount may be inconvenient or disturbing to the subject. A pneumatic device adapted to the finger plethysmograph and shown in Figure 8 permits the filter's manipulation by the experimenter who

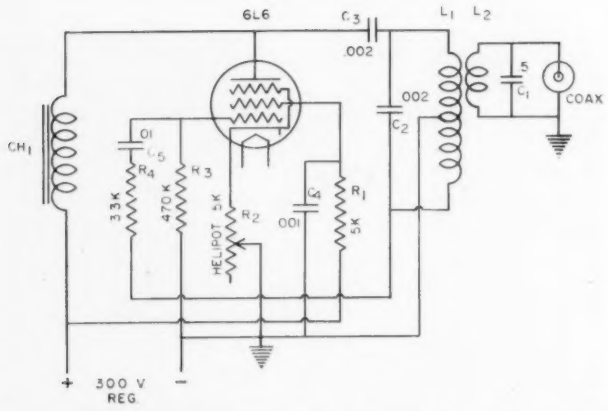

Fig. 6.—Modified Hartley oscillator for supply of 10 KC to the light bulb. CH_1 = Thordarson T20C52, 8Hy at 40 ma, 450 ohms; L_1 = 60 MH Air Core R.F. Choke Miller 693T, L_2 = 50 turn Pi wound over L_1.

may be at some distance from the subject, without disturbing the latter. The filter frame swings on an axis which is vertical to the plane of the figure. After having been pushed into place by the piston-plunger, it is returned to the original position by the spring (cut from a watch spring).

The validity of the calibration depends on whether F is always equivalent to a certain quantity of blood in a particular application of the photometer. The theoretical answer to this question awaits determination of whether an increment of blood behaves as a lateral extension of a black body or as a thickening of a thin film. Probably both effects obtain. Earlier calibration experiments[8] indicated that the result was a linear increase in opacity with rising blood content.

When arterial constriction occurs and the rate of perfusion diminishes, decrements occur simultaneously in the volume pulses and blood content of the tissue. Because of the dimensions of the different vessels making up a vascular bed, most of the change in blood content occurs on the venous side. However, one would expect the numerical value of the ratio, dP/dV (decrement in volume pulse/decrement in blood content), to alter markedly when the venous bed is exceptionally large, as in the nasal septum, or when venomotor responses dominate the plethysmogram, as may also be the case in the nasal septum.

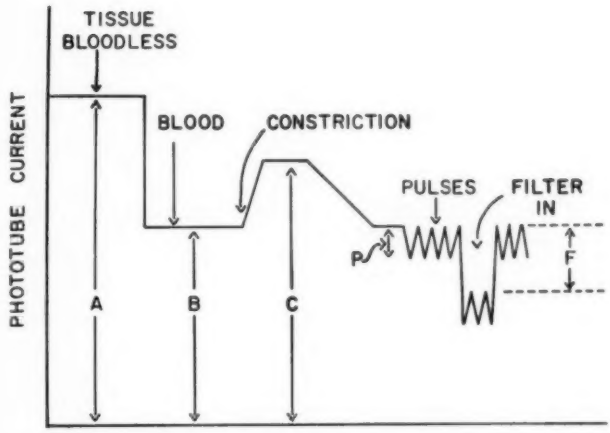

Fig. 7.—Schema illustrating the use of the glass filter in calibrating the photoelectric plethysmogram. Let A = the level of the phototube current when the tissue is bloodless; (A-B) = decrement due to entrance of an unknown amount of blood; (C-B) = increment in current due to constriction and exit of blood; P = decrement in current due to the volume pulse; F = decrement in current due to the insertion of the filter.

Reference to Figure 9 illustrates this point. The reduction in the blood content of the nasal septum, expressed in "filter units," was 3.1 times that in the finger pad. At the same time, the decrement in the volume pulse amplitude in terms of the control pulse (expressed in filter units) was 1.4 times greater in the finger pad. Although part of the quantitative difference in the decreases in the blood content of the nasal septum and finger pad is probably due to the inclusion of the two vascular beds on the two sides of the septum in the transillumination, the obvious difference in the ratio, dP/dV, in these two records indicates that this explanation is inadequate. The differences in behavior must also be due to the inclusion of effects from a relatively larger venous plexus in the nasal record.

The availability of this observational procedure for studying vascular responses of considerably longer duration is illustrated in Figure 10. The nude subject was seated in a crude climate chamber cooling of which began at "1" in Figure 10. The blood content and volume pulse amplitude decreased almost simultaneously in the finger pad and nasal septum. Reversal in these effects appeared on re-heating the chamber (at 3). However, recovery in the blood contents was

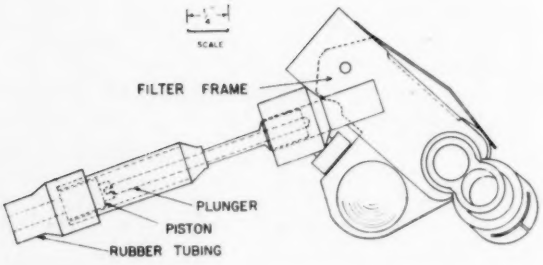

Fig. 8.—Pneumatic device for manipulating the filter mount. The filter frame is drilled with two holes (as in Figure 1), in one of which the glass plate is inserted. In the position shown, the empty hole is in the light path. The rubber tubing which may be any convenient length is connected to a pressure bulb to be squeezed by the experimenter.

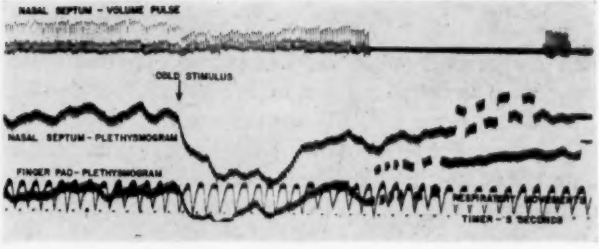

Fig. 9.—Simultaneously recorded photoelectric plethysmograms of the finger pad and nasal septum. Note the reduction in the blood content and the volume pulses of the nasal septum on the application of a cold stimulus. Measurements on the original records: F (nasal record) = 13.8 mm; F (finger record) = 20.4 mm; reductions in blood content: 3.22 and 1.03 filter units in nasal septum and finger pad respectively; changes in volume pulses: from 0.41 and 0.31 filter units to 0.21 and 0.09 filter units in nasal septum and finger pad respectively; i.e., at the height of constriction, the reduction in the volume pulse was 50 and 70 per cent in the nasal septum and finger pad respectively.

incomplete in both vascular beds. The promptness and synchronicity of the changes in the two structures suggest mediation by their vasomotor innervation. One may note again that the value of the ratio, dP/dV, differed markedly in the two vascular beds. We consider the difference to express the role of the septal venous plexus. We do not infer that the volume change necessarily demonstrated a venomotor response.

SPECTROPHOTOMETRIC CONSIDERATIONS

Particularly in the application to the nasal septum, much of the value and reliability of photoelectric plethysmography must depend on the influence of and correction for the spectral distribution of energy in the radiation incident on the photocathode in relation to the latter's spectral sensitivity. Several factors determine the current output of the phototube. These are: its spectral sensitivity, the spectrum and intensity of the light incident on the tissue, and the transmission characteristics of bloodless tissue and of blood. In a brief experiment, only the influence of the blood present in the transilluminated tissue may vary. Certainly, opacity increases with rising blood content. Whether it apparently increases likewise with reduction of oxy-hemoglobin depends on what photosensitive device views the transmitted light and the spectral range of the latter. In the instance of the S-1 photocathode viewing tissue transmission calculations from the transparency curves of reduced and oxygenated hemoglobin in solution, indicate that reduction or oxygenation of all of the hemoglobin would effect a change of about five per cent in the photoelectric current, in the absence of simultaneous change in blood content. This effect on the plethysmographic or volume pulse traces would be recognizable, but the actual magnitude of the "errors" would be less than a five per cent variation in the photoelectric current.

The possible extent of the implied error is probably a function of the amount of blood in the transilluminated tissue since in dilute suspensions of erythrocytes the extinction of light by hemoglobin is a small fraction of that due to scatter by the cells[9] as is readily demonstrable in test-tube experiments. If the calculated upper limit of the error is correct, it would be equivalent to about 0.5 filter unit (1 F.U. = .085 photoelectric current). This is appreciable but not serious as reference to Figure 9 will show.

In calibration experiments on the terminal phalanx of the finger, the volume pulses as traced by an optically recording plethysmograph correlated very well indeed with their equivalents in the simultaneous

traces made with the photoelectric plethysmograph, both in amplitude[8] and wave-form over a wide range of digital constriction and dilation. This observation would indicate that the amount of blood involved in photoelectric plethysmography of the skin is quite small and equivalent in photometric effect to that of a very thin cuvette layer since the studies of Kramer et al.[10] show that the opacity of moving whole blood in cuvettes thicker than 0.1 mm does not follow Beer's law. It is therefore probable that in the skin the extinction of light by hemoglobin is a minor factor in variations in opacity due to changes in blood content. Further, the rates of digital blood flow are usually so high in relation to metabolic requirements that, in the absence of arterial hypoxia, the ratio of HbO_2/Hb would alter only slightly with variations in flow.

The application of this argument to the nasal mucosa should be made cautiously. The extensive venous plexus there differs markedly in structure and dimensions from that in the finger. It is theoretically possible for an increase in arterial inflow to diminish opacity despite an absolute increase in blood content but the typical experiences illustrated in Figures 9 and 10 deny that such effects obscure the main features of the vascular responses in this mucosa. One may also note that the upstroke in the volume pulsation during which the ratio of HbO_2/Hb must increase, correlates in time with the upstroke in the photoelectric pulsation. If opacity were being reduced by an increase in their ratio, the reverse should be true.

RATE OF BLOOD FLOW IN THE SEPTAL MUCOSA

The calibrated amplitudes of the septal volume pulses as recorded in Figures 9 and 10 were of the same order of magnitude as those in the finger pad where very high rates of blood flow may obtain. One may test the implication that correspondingly high rates of perfusion exist in the nasal septum of the comfortable resting subject by calculating the rate of blood flow which is required to deliver the heat lost to the respired air.

Ordinarily, the processes of warming and humidifying the inspired air approximate equilibrium by the time that the incoming air reaches the trachea.[11] As a result of the character of the air flow along the nasal septum,[12] much of the aqueous and thermal exchange between the mucosa and the air must take place on the nasal septum. Although exact data do not appear to be available respecting the quantitative topography of these thermal transfers, one may estimate

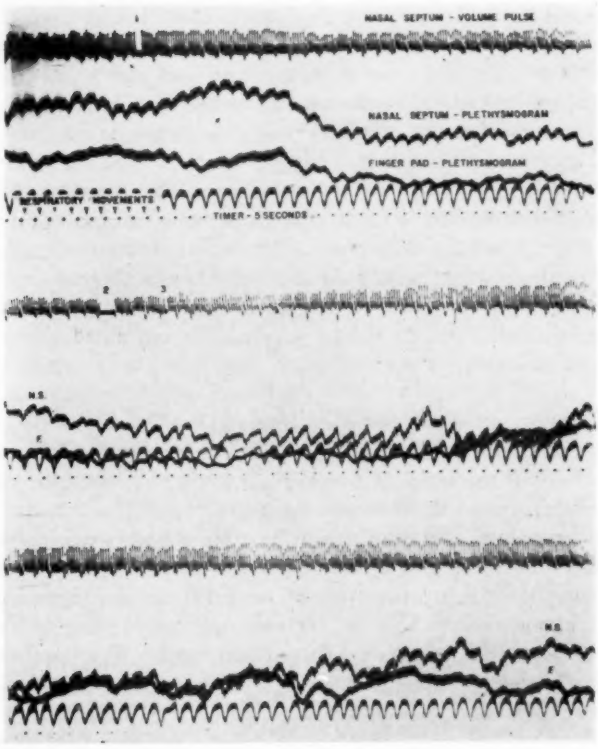

Fig. 10.—Simultaneously recorded photoelectric plethysmograms of the nasal septum and finger pad during cooling of the subject in a climate chamber. Cooler was turned on at 1, turned off at 2, and heaters turned on at 3. Measurements on the original records: control volume pulses = 0.21 and 0.34 filter units in the nasal septum (n.s.) and finger pad (f.p.); decrement in volume pulse = 0.09 and 0.26 F.U. in n.s. and f.p.; decrement in blood content = 3.0 and 2.1 F.U. in n.s. and f.p.

nevertheless the approximate rates of heat loss from the septal mucosa. Assuming that the respiratory heat loss was 6 KgCal/hour, that all of this took place on the septum, that the septal mucosa had a surface area, effective in this transfer, of 200 cm^2,[12] one obtains a rate of 0.5 gm cal/minute/cm^2 of mucosal surface (or 300 KgCal/M^2/hour). This rate is about five times as great as that which obtains over the skin surface of a resting subject.

Before utilizing this calculated rate of heat loss in estimating the rate of blood flow, one may ask whether this rate of septal heat loss is possible. If derived entirely from evaporation, it would require a continuous supply of water at the rate of 500 gm/M^2/hour. (Thermoregulatory sweating may readily exceed this rate.) Maintenance of a "moist" condition of the mucosa would require a high rate of secretion at this level of evaporation but secretion is not essential to the latter since the mucosa is freely permeable to the diffusive movement of water. Thus, in the dog's tongue the exclusion of saliva still allows evaporation to proceed at a rate which is about 75 per cent of that which would take place from a pool of water at the same temperature, i.e., the mucosa behaves as though 75 per cent of its surface was covered by a layer of liquid water. There is therefore no inherent difficulty which would prevent the estimated rate of heat loss from occurring.

One may then calculate the minimal rate of blood flow in the septal mucosa from the equation, blood flow = heat loss/(T_A — Tv) in which T_A is the temperature of the entering arterial blood and Tv the temperature of the effluent venous blood. (In the instance of the septum, physical conduction of heat from deeper tissue is scarcely available. Therefore, all of the heat transfer must be due to vascular convection.) Substituting appropriate values in the above equation, the calculated flows would lie between 0.5 and 0.2 ml/cm^2/minute, depending on the difference (T_A — Tv) used. These values are of the same order of magnitude as in the finger pad.[8] It would seem therefore that the volume pulse data are correct in indicating a high rate of septal perfusion even though the numerical flow equivalent of a given pulse amplitude cannot be stated at the present time. These correlations affirm the usefulness of the septal volume pulse as an index of septal blood flow.

SUMMARY

The application of the photoelectric plethysmograph to the nasal septum has been re-studied with respect to its mechanical design, spectrophotometric considerations and the analysis of its records of vascular responses in the nasal mucosa.

The design has been improved by incorporating a calibration procedure, by providing a more rigid and more comfortable mount for the apparatus which may be worn by the subject for long periods without discomfort, by operating the light bulb with a

Hartley oscillator and by monitoring the light emission with a photoelectric cell.

The calibration procedure permits comparisons of changes in the amplitudes of the volume pulses and in blood content during various vascular reactions. Changes in the rate of blood flow were inferred from changes in the amplitude of the volume pulses.

The changes in septal blood content appeared to be relatively and absolutely larger than those in the finger pad when various vasomotor responses were elicited. These differences were attributed to the participation of the relatively extensive venous plexus of the septum in the reactions.

The rate of septal blood flow appears to be of the same order of magnitude as that in the finger pad. This is inferred from the amplitude of the volume pulse and the estimated rate of septal heat loss.

Errors which might arise in a changing ratio of oxy- to reduced hemoglobin are discussed.

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XLVII

PERROTATORY NYSTAGMUS IN THE BALLET DANCER, PIGEON, AND BLIND PERSON

ITS APPLICATION AS A TEST FOR DIFFERENTIATING ORGANIC FROM PSYCHIC BLINDNESS

KURT TSCHIASSNY, M.D.

CINCINNATI, OHIO

The experiments described in this paper deal with optokinetic and otokinetic (vestibular) factors responsible for perrotatory nystagmus. I take the liberty of replacing the term "vestibular" by "otokinetic" (otokinesis) thus indicating phonetically the similarity of two reflexes resulting from two entirely different sources.

"Perrotatory" means during rotation in contrast to "postrotatory" which means after cessation of rotation.

The subjects of these experiments are: the ballet dancer, the pigeon, and the monocular blind person. Studies with the binocular blind person are not shown in the film. Such studies were instituted about five years ago and since then repeatedly demonstrated at clinical conferences in the departments of otolaryngology, and of neurology and in our routine clinical courses. I discussed them later in some courses at meetings of the Academy of Ophthalmology and Otolaryngology.

STUDIES WITH THE BALLET DANCER

When we watch carefully a ballet dancer performing her turns, the so-called "pirouettes," we will notice jerking movements of the head occurring rhythmically in short intervals during her spinning. These head jerks are not a kind of head nystagmus such as was shown by Ewald[1] to occur reflexly in pigeons and some other animals with lateral eyes, when rotated.

From the Departments of Otolaryngology and Physiology, College of Medicine, University of Cincinnati.

Presented at the meeting of the Academy of Ophthalmology and Otolaryngology, October 14, 1956.

In the dancer these head movements are intentionally produced and represent an integral part of her professional training. The ballerina is well aware of the importance of these head jerks in maintaining balance during and particularly when stopping the pirouette. The girls call this technique "spotting." The question why and how these head movements prevent postrotatory reactions puzzled Bárány[2] who considered a possible analogy with conditions in the pigeon as observed by Ewald. However, he could not explain it.

We approached the problem by decomposing the "pirouette" into its constituent parts. We appreciate in this matter the assistance and, as will be seen, the co-operation of Miss Geraldine Roberts, a member of the Department of Dance of the Cincinnati Conservatory of Music. Consulting some monographs on ballet dancing[3,4] provided additional information.

The first part of the picture deals with an analysis of the pirouette. As we learned from the ballerina, the dancer, before starting her turns, chooses an immobile object in front of her as a reference point; this she keeps in focus during the entire act.

To me the pirouette appears to consist of two phases. In the first only the body rotates. The head is fixed as if it were connected with the immobile reference point by an imaginary rigid link. While the body keeps on rotating as far as permitted by vertebral joints and ligaments the reference point which appears to move in the opposite direction is kept focused until the extreme limit of possible excursion is reached. At this moment the second phase appears as an additional rapid turn of the head in the direction of the preceding rotation of the body covering an arc of about 180°. Thus the reference point is focused again in front of the dancer. The cycle is now completed and may be repeated as before.

The question which confronts us, is: is it possible that during these two phases semicircular canal stimulation takes place and, if not, why not?

As you know, the canals are stimulated by cupula displacement which in the case of rotation depends on inertia due to acceleration or retardation of rotation of the head; of course, of the head, but not of the body. Since there does not exist any head rotation during the first phase any possible cupula displacement can be ruled out. In the second phase a brief and rapid head rotation occurs. Dohlman[5] in his beautiful experiments on the pike has shown the absence of

cupula displacement upon brief rotation of the head. As he explained it, acceleration when rotation starts, and retardation when it stops are forces opposing and neutralizing each other when appearing within a brief interval.

It is logical to assume that identical factors are operating during the second phase of the pirouette. Therefore, whenever the pirouette is stopped, the cupula remains in its resting position and therefore stimulation of the semicircular canals is absent.

The importance of spotting for maintenance of balance is shown by comparing the appearance of the dancer when spinning alternately with and without spotting. In the first case, when she stops her turns, there is no imbalance or past-pointing, while she is evidently imbalanced when she stops spinning without spotting.

Another simple proof, to the same effect, is shown when the dancer is rotated on the revolving chair alternately without and with spotting. The reference point is placed in front of her. When she is rotated in the usual way without spotting postrotatory responses appear. These include past-pointing and nystagmus. The latter is small and of short duration probably due to some professional adaptation. Contrariwise, when rotation with perrotatory spotting is stopped, no past-pointing or nystagmus appears. A similar experiment was anticipated by Bárány[2] and is mentioned by Mowrer[6] with reference to Griffith.

EXPERIMENTS WITH THE PIGEON

Ewald, as mentioned, has shown in the pigeon the presence of head nystagmus during rotation with absence of postrotatory nystagmus. However, when he blinded the pigeon head nystagmus during rotation was absent while a distinct postrotatory head nystagmus appeared. We duplicated Ewald's experiment with a minor modification. Instead of blinding the pigeon we only blindfolded the bird with a piece of adhesive. The results were the same.

There exists evidently a striking analogy between conditions in the dancer when spotting while spinning and the pigeon's head nystagmus when being rotated:

1. In both postrotatory responses do not occur subsequent to rotation with simultaneous head movements, such as intentionally produced by the dancer when spotting, and reflexly in the pigeon.

2. In both postrotatory responses do occur subsequent to rotation without perrotatory head movements.

3. In both perrotatory head movements are under visual control.

Moreover, it was shown that in the pigeon elimination of vision abolished the perrotatory head nystagmus. Therefore, it appears that in the pigeon perrotatory nystagmus depends predominantly or even exclusively on vision, while labyrinthine stimuli per se in the absence of vision do not produce perrotatory nystagmus of an appreciable degree.

EXPERIMENTS WITH THE BLIND PERSON

In man perrotatory nystagmus is known to be the combined result of both optokinetic and otokinetic stimuli. It was shown by Bárány,[2] Brunner,[7] Ohm,[8] Bartels[9] and others and particularly by Cemach and Kestenbaum[10] that in men the visual factor in perrotatory nystagmus dominates the vestibular factor. The latter authors have shown almost normal perrotatory nystagmus present in cases of complete bilateral vestibular paralysis. We have seen its presence in patients subsequent to meningitis and streptomycin intoxication in the absence of any vestibular function.

It was a challenging problem to determine the part contributed to perrotatory nystagmus by the otokinetic component. For this purpose vision had to be eliminated. Application of Ewald's modified experiment to man was a severe technical problem. Of course, blindfolding the patient or rotating him in the dark or with his eyes closed eliminated vision. But these procedures prevented observation of eye movements. Nystagmographic devices were not available to me. For these reasons we studied conditions in patients with complete binocular blindness. We noticed perrotatory nystagmus regularly present when rotation was started. The intensity was less than in the sighted person, gradually decreasing until nystagmus completely disappeared. This took as a rule less than ten rotations, and sometimes only one or two. We succeeded, however, in establishing a close analogy between conditions in man and Ewald's experiment with the blinded pigeon by experimenting with monocular blind persons. In these cases vision of the patient can be completely eliminated by blindfolding only the sighted eye, while nystagmus can be observed by watching the uncovered blind eye. A patient of ours became blind in the right eye with a temporal defect in the left subsequent to a basal

skull fracture. There is normal nystagmus during rotation with both eyes open. It disappears when the patient covers the sighted eye with his hand and reappears when he uncovers it. Of course, postrotatory responses are present even with the sighted eye covered. When rotation is started with the sighted eye covered, nystagmus with gradually decreasing intensity appears; it disappears after several rotations but reappears when the sighted eye is uncovered. From these studies it becomes evident that in man nystagmus during rotation depends predominantly but not exclusively on optokinetic factors. Its unrestricted persistence during rotation proves presence of vision, its gradual decrease and final disappearance proves blindness.

Rademaker and Ter Braak[11,12] differentiated two types of optokinetic nystagmus, a cortical or active and a subcortical or passive. In the former, only a part of the visual field is rotating. Its appearance depends on attention directed to the moving object. It can be easily prevented by shifting attention to resting objects. In the subcortical type the entire panorama is moving. It is independent of cortical influences. Scala and Spiegel[13] have shown its presence after removal of both hemispheres when only the superior colliculi were kept intact.

The optokinetic drum nystagmus is an example of the cortical type. Its use as a test for differentiating between organic and psychic blindness, as repeatedly mentioned in the literature, is unreliable and discouraged by Walsh[14] since it depends on the co-operation of the subject. Contrariwise the optokinetic nystagmus induced by rotating the subject on the Bárány chair, as shown in our studies, represents the subcortical type which cannot be suppressed by any cortical impulses. Its gradual disappearance during rotation indicates complete organic blindness which is binocular when occurring without and monocular when occurring with covering of one eye. I call this procedure "the perrotatory nystagmus test for blindness." We used it in a few cases, to the satisfaction of the attending ophthalmologists and neurologists. Studies concerning its evaluation in infants are in progress.

Two cases of particular significance are briefly reported:

REPORT OF CASES

CASE 1. This is an abstract from the original report given at the surgical death meeting, December 18, 1953.

A sixty-four year old white male was admitted on November 27, 1953, with a history of having fallen down four steps, landing on his left occiput. There was bleeding from the left ear. From the previous medical history we learn that the patient was admitted here in August 1953 because of blindness of ten weeks' duration. He was studied but his problem was never definitely pinpointed. Cerebrospinal fluid never showed a positive Wassermann. Serologic test for syphilis was positive consistently and he was treated with nine million units of penicillin. The final diagnosis was some unusual form of meningovascular lues. In the interim he had intermittent periods of disorientation. Although he appeared completely blind he had light perception at that time (August). This is no longer present.

Neurological examination revealed an euphoric disoriented man who gave the impression of exaggerating his complaints. Pupils were equal at 5 mm and fixed to light. The patient claimed to be blind and did not react to visual threats. The fundi showed pale gray discs with fuzzy borders but no edema and no true white discs. Maculae were not remarkable. Skull films were negative. Impression on admission was: blindness of unknown etiology or a meningovascular lues or frontal lobe tumor. Basal skull fracture with left otorrhea. He was seen by ophthalmologists who believed that the patient did have bilateral light reflex to very strong stimuli. However, they felt that it could not be determined whether he was really blind. He seemed not to have the usual attitude of a blind patient. An electroencephalogram on November 30 revealed no change over the previous reactions in August 1953, which showed a diffuse slow dysrhythmia. During his stay in the ward the patient would get up and walk around the ward. He was able to select from the tray the foods that he wanted. There were many factors in his attitude that strongly suggested that he was not blind.

However, on December 9, 1953, he was seen by Dr. Tschiassny in the ear, nose and throat clinic who by tests with the revolving chair determined that the man was truly blind. On the following day therefore, an electroencephalogram was done which showed a definite frontal lobe defect, predominantly on the right side and apparently arising from the base of the frontal fossa. On December 11 a craniotomy was done and a meningioma discovered which was partially removed. It apparently arose from the olfactory groove on the right side but extended into the frontal fossa on the left and displaced both frontal lobes. Tracheotomy became necessary. The patient died on the second postoperative day.

CASE 2. A 35 year old man was transferred from the Cincinnati Jewish Hospital as a "police hold" on January 2, 1955. The patient stated that he slipped on the ice three weeks ago injuring the back of his head. This was apparently a minor injury, but the patient went to the Jewish Hospital where he was admitted for neurosurgical observation. Physical examination at that time was unrevealing. Skull x-ray showed a questionable fracture in the left parictotemporal region. He was discharged after one week. At home he had what he called a "little seizure" and because of this he returned to the Jewish Hospital and was readmitted. There he had several seizures, none of them in the presence of a doctor. After two weeks the police notified the Hospital that the patient was wanted in Louisville (Ky.) and the patient was then transferred to the Cincinnati General Hospital under police guard. While the patient was being admitted he suddenly fell to the floor. He stated that he could not see. Physical examination was entirely negative. Skull films showed a probable fracture in the left temporoparietal region. Lumlear puncture was negative. Pupillary reflex was present, but the patient stated that he could not see. An electroencephalogram was made and reported as normal. The genuineness of the blindness and seizures was questioned. Therefore, the author was asked to evaluate the patient's vision by his "rotatory nystagmus test." This he did proving that the patient was not blind but had, at least, light perception. This the patient admitted, following the author's statement but not before. With this information psychiatric consultation was requested. The psychiatrists were able to show by means of a pentothal interview that the patient could see. The patient was discharged February 8, 1955.

SUMMARY

These two case reports illustrate the use of the perrotatory nystagmus test for blindness. In the first case the organic character of the blindness is revealed, in the second case psychic blindness is unmasked. The development of this test represents to some extent an unforeseen practical application arising as a side effect from a primarily academic study. A clinical utilization of nystagmus during rotation is shown for the first time.

101 LOUIS AVENUE

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XLVIII

PEMPHIGUS OF THE LARYNX

G. Obregon, M.D.

Iowa City, Iowa

Pemphigus of the larynx, although relatively rare, is of great importance to the laryngologist because the larynx may be the first site of the disease; this has been reported on several occasions.[1-4]

The advent of the Tzanck Test,[5] the "cantharides test,"[6] has simplified the diagnosis and corticosteroid therapy has improved the treatment of pemphigus. Before these tests and therapy were available the otolaryngologist found it difficult to establish a diagnosis of laryngeal pemphigus in cases with absence of cutaneous lesions, and any available therapy frequently failed to arrest the condition.

Pemphigus can be divided into four main types: pemphigus foliaceus, erythematosus, vegetans and vulgaris.[7]

Pemphigus foliaceus is characterized by an extensive exfoliative type of dermatitis. The mucous membranes show little or no involvement.

Pemphigus erythematosus or Senear-Usher syndrome is recognized by erythematous, scaling, crusting lesions of seborrheic appearance on the nose and malar areas in a butterfly distribution. Other areas of the body are also involved but the mucous membranes are seldom affected.

Pemphigus vegetans may have its initial bullous lesions on the oral mucous membrane, spreading later to numerous areas of the body. The bullae lead to erosions, and areas of hypertrophic vegetative granulation tissue slowly develop upon these denuded areas. The vegetative lesions characteristic of this type of pemphigus are more commonly seen on the skin than on the mucous membranes except for the vermillon border of the lips.

From the Department of Otolaryngology and Maxillofacial Surgery, State University of Iowa, Iowa City, Iowa.

The laryngologist is mainly concerned with the fourth type of pemphigus, pemphigus vulgaris, because the disease may manifest itself first in the larynx. Pemphigus vulgaris is seen in adults and is rarely if ever seen in children or adolescents. There is no sex predilection but the Jewish race is reported as more commonly affected. The area most frequently involved is the trunk followed very closely by oral lesions.[8] One author reported[3] 29 cases of pemphigus and 19 of them had primary oral lesions. Another[12] disclosed that 14 out of 23 patients developed pemphigus primarily of the oral mucosa. The time lapse for the cutaneous lesions to appear in those patients with primary involvement of the mucous membranes of the mouth ranges from a few weeks to three years. It is believed that this interval is of prognostic significance, the more serious the case the earlier the appearance of the cutaneous lesions.

The patient with laryngeal pemphigus may seek the advice of a laryngologist because of hoarseness which is often the sole initial complaint.[9] Other later symptoms are dyspnea, odynophagia, otalgia, and productive cough. One of our patients reported coughing up bits of sloughing tissue. Constitutional symptoms are sometimes present.

On indirect laryngoscopy, the typical bullae filled with serous fluid alternating with denuded areas (resulting from ruptured bullae) of an intense red color are seen. In older cases typical contracted scars are visualized. Some[10] have attributed a great deal of clinical significance to this scarring because "most lesions with which pemphigus might be confused do not leave scars." The scarring is so severe that it quite often gives origin to varying degrees of laryngeal stenosis.[4]

The histologic pathological features of pemphigus are fairly characteristic.[11] The main histopathological finding in pemphigus has been referred to by Civatte as acantholysis. This is fundamentally a disturbance of epidermal cells in which there is a disruption of the intercellular bridges in some areas. The acantholytic or Tzanck cell shows a rounded, sharply defined and deeply stained cytoplasm. The nuclei may be rounded, swollen, and hyperchromatic. This picture is diagnostic for the entire pemphigus group, which includes the previously mentioned types. However, certain authors[12] divide pemphigus vulgaris into two subgroups, the pemphigus vulgaris acutus and the pemphigus vulgaris chronicus. This distinction is based on the clinical course of the disease, the predominance of oral lesions in pemphigus vulgaris acutus and the absence of acantholysis in the pemphigus vulgaris chronicus.

The diagnosis of pemphigus has been greatly simplified by the relatively recent demonstration of the specific and characteristic histologic patterning of the pemphigus group. With the use of the Tzanck Test or the Cantharides test[6] one does not have to wait for the skin lesions to appear in order to make a definite diagnosis and to institute therapy. (The Tzanck Test is performed on the fluid obtained from a vesicle. A smear is made and processed in the same way as a routine blood smear using Giemsa's stain. The Cantharides test may be performed according to the following technique: Cantharides cerate N.F. is used as a vesicant, a small sample measuring 4 by 4 by 2 mm is placed on an elastic bandage (Band-Aid). The patch is applied on apparently normal skin of the forearm and left in place three hours. An excision biopsy of the artificial bulla is done and the wound is closed with two silk sutures. The specimen is fixed in formalin and stained with hematoxylin-eosin for microscopic examination.) Previously such delay resulted in irreparable laryngeal damage in a certain number of cases. Before the corticosteroids were introduced some patients with oral pemphigus could be maintained in a state of remission by the administration of Acetarsone (stovarsol). We have in our records a patient with oral pemphigus who has been maintained in a state of remission with this medication for five years.

Recently we have been using corticosteroids in pemphigus therapy with excellent results. With judicious use of cortisone, prednisone, or corticotropin systemically, a great number of remissions can be induced. The initial daily doses ordinarily are quite large and vary from 200 to 500 milligrams of cortisone or from 40 to 80 units (milligrams) of corticotropin given intramuscularly. The dose of cortisone may be gradually diminished over a period of weeks or months and the maintenance dosage of corticosteroids is dependent upon the clinical response. This dosage may be found to be precise and doses very slightly below the optimum level will rapidly result in the reappearance of the lesions.

The following report of two cases of pemphigus of the larynx seen in our clinic shows some of the difficulties in the diagnosis and some of the complications of this disease.

REPORT OF CASES

CASE 1. A 77 year old white female was referred to our clinic on October 6, 1956, with complaints of occasional blood streaked

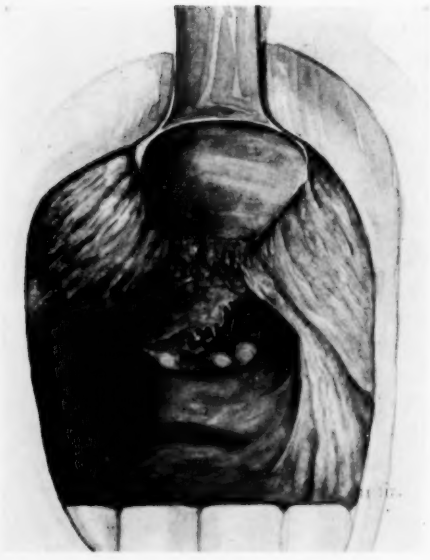

Fig. 1.—View of the epiglottis on suspension laryngoscopy. The blebs and denuded areas are well demonstrated.

sputum for one year, odynophagia for three to four months and coughing up pieces of tissue for the past six months. Her past medical history revealed that this patient was a known diabetic for the last three years but that her diabetes was under control. Her medical history was otherwise negative.

Physical examination revealed an obese white elderly woman of stated age and in no apparent distress.

The hypopharynx revealed a bleb about ½ centimeter in diameter on the posterior pharyngeal wall at the level of the epiglottis, and three smaller blebs were noted in the larynx. Two, about three to five millimeters in diameter, were located on the rim of the epiglottis and the other one on the right aryepiglottic fold. Numerous raw areas which appeared to be denuded of epithelium were also noted in the larynx and hypopharynx. The laryngeal dynamics were within normal limits and no impairment in the airway was noted (Fig. 1).

The remainder of the physical examination was essentially negative.

Laboratory Data. The urine, complete blood cell count and differential count, sedimentation rate, bleeding time, coagulation time, blood chemistry, plasma protein determinations, Wassermann, skin test for chronic granuloma, and x-ray of the chest were either within normal limits or negative.

Hospital Course. On November 12 the patient had a laryngoscopy and biopsy. The findings previously noted on indirect laryngoscopy were corroborated and a biopsy was taken from one of the areas of superficial ulceration. Half of the specimen was sent to the pathologist for histological study and the other half to the bacteriologist for cultures.

The material that the patient was coughing up during her hospitalization was subjected to microscopic examination. The pathologist reported evidence of chronic inflammation from the tissue submitted. The culture revealed normal flora.

The Department of Dermatology was called in consultation and concurred with the clinical diagnosis of pemphigus of the larynx and carried out a cantharides test on the left forearm; a biopsy was taken from this area three hours later. The biopsy showed numerous acantholytic cells characteristic of pemphigus. By the time a diagnosis had been established the patients' lesions had healed spontaneously. She was given no medication but was told to return if she had symptoms of recurrence so that we could establish a base line for corticosteroid therapy.

CASE 2. A 34 year old white female was seen in our clinic on September 10, 1954, with the following complaints: intermittent appearance of blisters in the mouth and palate of one year's duration; marked nasal crusting, epistaxis, occasional hemoptysis. Odynophagia, persistent hoarseness, and slight dyspnea had been present for the previous three weeks. The rest of her medical history was essentially negative.

Physical examination revealed a well developed and well nourished white female of stated age in no apparent distress. Marked nasal crusting and dried old blood were noted, the nasal mucosa appeared edematous but no tumors were noted. Three small vesicles,

three to four millimeters in diameter, were seen on the soft palate. The larynx showed two small white vesicles four to six millimeters in diameter on the rim of the epiglottis and several denuded areas over the right false cord that appeared to the examiner as if they "had been burned." The true cords were not visualized in their entirety; however, the laryngeal dynamics appeared normal. The laryngeal airway was reduced to half of its normal size. The rest of the physical examination was essentially negative.

Laboratory Data. The urine, complete blood cell count, sedimentation rate, blood chemistry, Wassermann, skin test for chronic granuloma, allergy investigation and x-rays of the chest and sinuses were either within normal limits or negative.

Hospital Course. A tentative diagnosis of pemphigus vulgaris was made. However, at the time we had no knowledge of the Tzanck Test and Cantharides Test and we were unable to substantiate our clinical impression. The patient was referred to the Department of Dermatology where a tentative diagnosis of recurrent aphthous ulcers was made. Material obtained from one of the palatal vesicles gave no specific information. Because of marked reduction in the airway a tracheotomy was performed in October of 1954 followed by a direct laryngoscopy and biopsy. The specimens were obtained from the right false cord and were submitted for pathological and bacteriological examination. Respective impressions were granulation tissue of the larynx and normal flora.

Our clinical impression was pemphigus vulgaris of the larynx.

The patient was given 150 mgs of cortisone daily with prompt disappearance of the laryngeal lesions and marked improvement in the airway. The tracheotomy tube was removed in December, 1954, and the dosage of cortisone was reduced to 100 mgs. At the present time the patient is taking 25 mgs of cortisone daily. During all this time we have periodicaly discontinued cortisone therapy and have stimulated adrenal cortical function by the use of ACTH for periods of two to three weeks.

The last time the patient was seen (December 12, 1956) it was noted that the right vocal cord was fixed and there was a minimal amount of laryngeal stenosis. However, the patient's voice was slightly hoarse but she has no difficulty in breathing. No new lesions have been observed during her treatment with corticosteroids for almost two years.

SUMMARY

1. The different types of pemphigus are briefly reviewed.

2. Emphasis is placed on the appearance of pemphigus in the larynx as the first site of the disease.

3. The histological appearance of the lesions of pemphigus is given.

4. The Tzanck and Cantharides Tests are discussed as diagnostic aids in pemphigus.

5. The diagnosis and treatment of two cases of laryngeal pemphigus are described.

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XLIX

AVOIDING INJURY TO THE EXTRALARYNGEAL NERVES

RALPH L. GREGG, M.D.

SEATTLE, WASH.

In 1932, Lahey[1] made a singularly astute observation regarding the occurrence of sudden respiratory difficulty in a patient undergoing thyroidectomy. He theorized that such sudden respiratory emergency was precipitated by injury to the abductor components only of the recurrent laryngeal nerves on both sides, leaving the adductor fibers intact.

Just such an occurrence in our experience in 1946 influenced us, King and Gregg,[2] to set up a series of nerve dissections on cadavers in an effort to better understand the mechanism of this tragedy. The actual cadaver dissections of the extralaryngeal nerves gave us a lead to an anatomical reason for various behaviors of paralyzed vocal cords but did not give conclusive evidence. Merely because the recurrent laryngeal nerves were found on occasion to divide into supposedly abductor and adductor branches within the danger zone of thyroid surgery, was not sufficient evidence to conclude that we had actually tied off only abductor nerves on the patient. It was indeed a thrilling conjecture, but lacked proof.

If we can rely upon the various types of vocal cord paralysis produced in dogs as representing their counterparts in man (and we believe it is acceptable), the following example is given as proof of Lahey's stated theory:

November 8. The recurrent laryngeal nerves were isolated on this experimental dog and the point of division into abductor and adductor branches located. The abductor nerves were tied off on both sides. Laryngoscopic examination revealed the cords lying close to the midline. The dog then experienced considerable respiratory difficulty. Pictures were taken to reveal the change in position from that of normal to bilateral abductor paralysis (Fig. 1).

December 14. The dog is unable to bark and cannot exercise without severe dyspnea. Laryngoscopic examination reveals the cords to be near the midline but the

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Work on dogs done at the Department of Physiology, University of Washington School of Medicine, Seattle, Washington.

opening of the glottis is a little wider than when examined two weeks ago. Anesthesia does not cause increase in respiratory effort (Fig. 2).

February 8. Dog returned to surgery, anesthetized and laryngeal examination made. The vocal cords were only slightly separated. No abduction function could be found. This represents a case of pure bilateral abductor paralysis and has been reproduced on other dogs, three of which died immediately after surgery (Fig. 3).

Such an experiment carried out on a patient would undoubtedly result in the death of the patient unless tracheotomy followed immediately. It is possible that such an occurrence has been signed out under the heading, "tracheal collapse," at some time or another.

The report[2] we made in 1948 regarding the possible explanation for various positions assumed by vocal cords following injury to extralaryngeal nerves was based on cadaver dissections and unfinished work on laboratory animals. It seemed to stimulate local interest in the problem of laryngeal paralysis, both as to prevention and to cure. Closer attention has been paid to the location and varying positions of the recurrent laryngeal nerve in thyroid surgery and as to the advisability of routine visualization of the extralaryngeal nerves to avoid laryngeal paralysis.

For many years Lahey has taught that the course of the recurrent laryngeal nerve is quite definite with its relation to the branches of the inferior thyroid artery, running as it often does through the branches or just outside of the artery before it branches. There is no doubt in our minds regarding the accuracy of this concept and we agree that wide dissemination of this knowledge is essential and that if surgeons everywhere will acquaint themselves intimately with this minute anatomy they will avoid an occasional laryngeal paralysis when all other precautionary methods would fail.

Prior to setting up the experiments for laryngeal paralysis on dogs, we did not agree with Lahey nor did we perform routine dissection of the recurrent laryngeal nerves in subtotal thyroidectomy. Many months had been spent on cadaver dissection and study of the varying positions and divisions of the extralaryngeal nerves but still we were not convinced of the wisdom of Lahey's teachings. We undertook the laboratory experiments on dogs[3] to prove the theory that the recurrent laryngeal nerve branches previously noted to occur near the inferior thyroid artery were actually those individual nerves supplying the adductor muscles, or separate from this, the abductor muscle on the same side. The operations on the dogs were made at

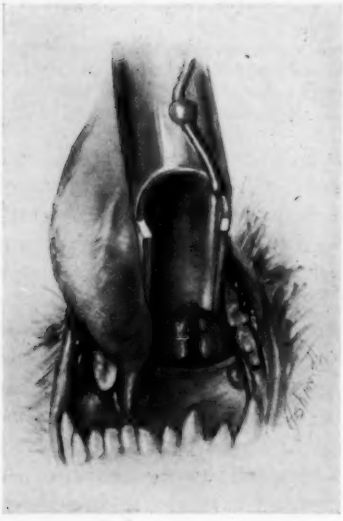


Fig. 1.—Bilateral abductor paralysis. Dog No. 10, Nov. 8.

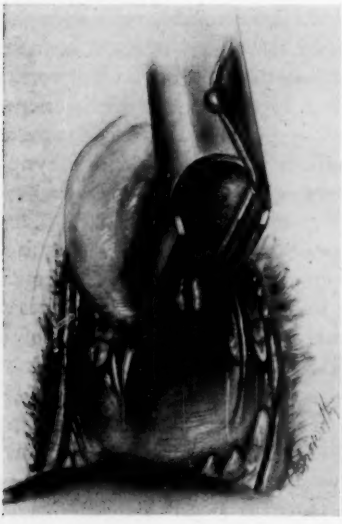


Fig. 2.—Dog No. 10, Dec. 14.

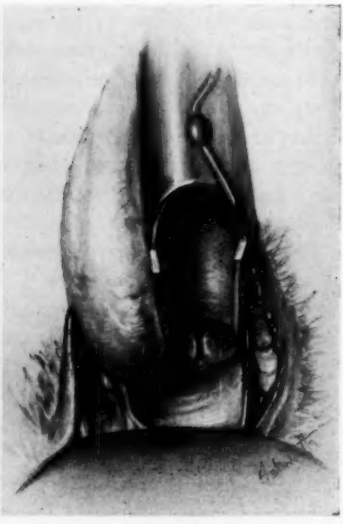


Fig. 3.—Dog No. 10, Feb. 8.

weekly intervals and carried on over a period of nearly three years. Thus we were able to follow the results of paralysis from injury to the various branches of the laryngeal nerves for sufficient length of time to tell if they were temporary or permanent. Shortly after starting these experiments we began routine dissections of the recurrent laryngeal nerves daily upon the thyroid patients, and were able to compare the nerves in the patients with those in the laboratory animals. There was a striking resemblance in appearance, size, consistency and mode of division of the nerves in the dog as compared to those in man. When the main trunk of the recurrent laryngeal nerve in the dog was elevated from its bed, it was noted to be surrounded by a sheath. A strong light passed through it showed the nerve trunk to be divided into two main divisions throughout the length of the sheath. Small sensory branches take off the main trunk at various locations in the neck but the two main divisions remain to leave the sheath as two individual nerves that go separately to the cricoarytenoideus lateralis and cricoarytenoideus posterior muscles. In some instances the divisions took place low in the neck; in others, just before the nerves entered the larynx or muscle bodies. In the majority of the dogs it was very easy to locate the divisions of the recurrent nerve sufficiently far from the muscle so that they could be tied off, severed from the trunk and retained for stimulation at varying intervals while the larynx was being examined for signs of paralysis of the muscles or position of the vocal cords. At the same time we observed that the recurrent laryngeal nerve trunks in the thyroid patients could be transilluminated to reveal two distinct nerves within the sheath of the nerve trunk. These two nerves could be followed to a point of division at varying levels usually posterior to the thyroid gland and seen to enter the larynx separately. On occasion, one or both of these nerves would divide once or twice before disappearing into the larynx.

In the dogs, it was a simple matter to determine which nerve supplied the adductor or the abductor muscle. Very fine stimulation from an electrodyne was used on the branch selected while the vocal cords were observed with a laryngoscope. However, no matter how small the stimulation, if applied to the recurrent laryngeal nerve trunk when all laryngeal nerves are intact, bilateral adduction resulted with the vocal cords coming together in the midline. Various simple techniques were devised to circumvent this. Injury to the contralateral recurrent laryngeal trunk will prevent bilateral adduction with unilateral stimulation. Unilateral adduction could be demonstrated by severing the adductor nerve from the laryngeal trunk and

Fig. 4.—Case 1.

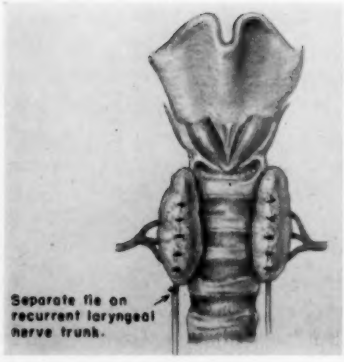


Fig. 5.—Case 2.

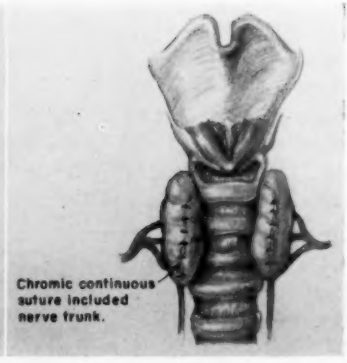


Fig. 6.—Case 3.

Location of sutures found post-surgically after realizing vocal cord paralysis present.

then stimulating the remaining adductor nerve. This could also be done with the abductor nerve on one or both sides. Injury by crushing at various points along the nerve trunk or its branches could be used as adequate blocking agent. It was found that, by and large, none of the little nerve twigs or branches given off the nerve trunk below the thyroid space could be stimulated to give either adduction or abduction of the vocal cords. Also, it was found that it was no problem to determine when one had selected either the abductor or adductor branch of the laryngeal nerve trunk by gross inspection, and that the adductor nerve was always larger than the abductor. Comparing the ease with which we could distinguish the main nerve trunk and the adductor and abductor branches in the dog with those dissected in thyroid surgery, the conclusion was drawn that, with very little experience, a surgeon could tell if he was dealing with the entire recurrent laryngeal nerve, its two main divisions, or just a small branch off the trunk or off one of the divisions. The point being that any surgeon interested enough to do routine dissection and visualization of the recurrent laryngeal nerve could, with a little experience, tell whether or not he was dealing with the whole nerve or just a portion. If he has the whole nerve before his vision, he is well on the way to avoiding laryngeal paralysis. Thus, though we had persisted in disregarding Lahey's advice, we eventually came to use and depend upon his technique.

Results from the use of the electrodyne in thyroid surgery were very disappointing. When the abductor branch of the recurrent nerve was stimulated on a patient, we obtained only adduction. Nevertheless, on the one patient in whom we had injured the adductor nerve, stimulation of the recurrent laryngeal nerve trunk on that side no longer resulted in bilateral adduction, but unilateral abduction and contralateral adduction. If we had been allowed to crush the recurrent nerve trunk on the same side, then according to similar results on the dog we would have obtained unilateral abduction only, by stimulating the abductor nerve distal to the point of injury.

It is not meant to infer that innervation crosses from one side of the larynx to the other at the levels of the larynx but rather that the stimulation takes a circuitous route and comes back down the opposite vagus, when one stimulates central to the point of injury or an uninjured nerve. We reproduced this identical injury on a dog and obtained unilateral adduction paralysis with loss of function in the cricoarytenoideus lateralis muscle resulting in very poor bark tone. It is just as important for a dog to have full use of his adductor muscles to enable him to bark as it is for a patient to have normal adductor

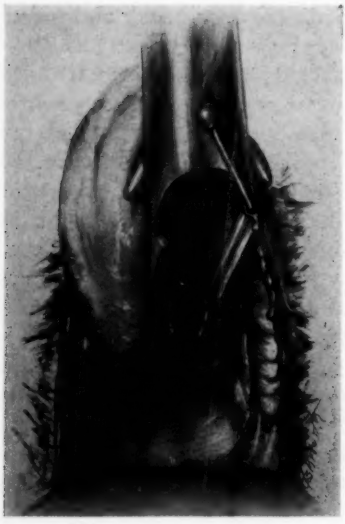


Fig. 7.—Dog No. 13, Nov. 23.

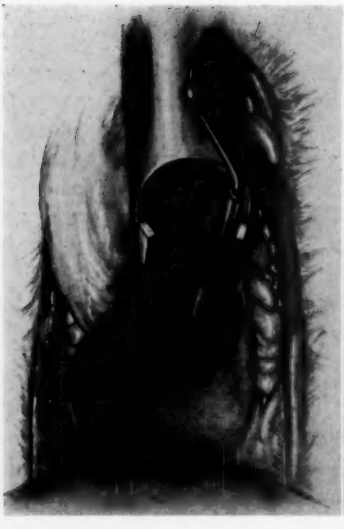


Fig. 8.—Dog No. 13, Dec. 21.
No bark tone; good airway.

Fig. 9.—Dog No. 13, Feb. 8.
Unable to bark; good airway.

muscles for singing. So much emphasis has been placed upon abductor paralysis in the literature that insufficient thought is given to the results of adductor paralysis. A preacher without both adductor muscles in good order is frustrated indeed. A saleslady with previous surgery for substernal thyroid tumor demonstrates a unilateral adductor paralysis. She comes in weekly, inquiring how soon her voice will be strong enough to carry her through a full day; by midafternoon her voice gets so weak and husky that she has to quit talking.

Prior to instituting routine dissection of the recurrent nerve on the thyroid patients, in spite of greatest caution and certainly many years of experience doing subtotal thyroidectomies particularly by the senior surgeon (King — at that time estimated in excess of 8,000 thyroidectomies), an occasional case of laryngeal paralysis resulted. During the one year previous, we had three outstanding examples of paralysis and three unilateral paralysis without symptoms. During this period when we did not isolate the recurrent laryngeal nerves, we operated under local anesthesia with some nitrous oxide and oxygen so that the patient could be partially awakened. The voice tone was used exclusively to determine if any degree of paralysis had occurred during the operative procedure. It was routine to waken the patient at the conclusion of each hemithyroidectomy and test the voice. On two occasions, one before the neck was closed, the other as the patient was being moved from the surgery, it was discovered that noticeable hoarseness was present. On a third occasion, shortly after the patient was returned to her room, the voice changes were obvious. In all three instances a search was made for the cause of the paraiysis and the recurrent nerve trunk found to be included in chromic suture that was meant for a vessel off the inferior thyroid artery (Figs. 4, 5 and 6). In one of these, the recurrent laryngeal nerve trunk was pulled up into a knuckle as it passed through the branches of the inferior thyroid artery and was tied doubled up. With the release of the suture, we felt there was immediate improvement in the pitch of the voice. Although the patient was hoarse for a few days, no permanent paralysis developed. These were too close for comfort and would probably have been avoided entirely had visualization of the nerve been done. It is impossible to leave sufficient gland to protect all nerves, and it is possible that we had more than the six known instances of unilateral paralysis, for at that time we did not routinely observe the vocal cords postsurgically.

The first year after instituting routine dissection of the recurrent laryngeal nerves following standard routine subtotal thyroidectomy we learned, among other things, that routine dissection of the nerve

Fig. 10.—Dog No. 8, Sept. 21. Bilateral recurrent laryngeal nerve trunk paralysis. Unable to bark; adequate airway.

Fig. 11.—Dog No. 8, Nov. 16. Still unable to bark; adequate airway.

Fig. 12.—Dog No. 8, Dec. 21. Able to bark; not adequate airway; signs of suffocation.

is fairly easy, that (as pointed out by Lahey[4,5]) the relationship of the inferior thyroid artery is quite constant and that the main trunk divides into two definite branches occasionally as low as the lower one-third of the thyroid gland, and on occasion these branches will pass one on either side of the artery. We also learned to expect more variation in location on the right side than the left, the left nerve being more constantly found in the tracheo-esophageal groove, now and then being elevated by passing through branches of the inferior artery.

After establishing the Lahey technique over 400 patients were operated on for thyroid disease before encountering a single case of either unilateral abductor, adductor, or mixed type of laryngeal paralysis of a permanent nature. These patients were all examined by laryngeal mirror before and after surgery and most of them were followed for from six months to a year postsurgically. It has not been necessary to re-examine the neck for possible suture on the recurrent nerve on a single patient on whom the recurrent nerves have been dissected and visualized. Further, there has been no instance of postsurgical laryngeal paralysis on these patients, as far as we know, resulting subsequently from scar tissue.

Seven patients operated on within the past two years for carcinoma of the thyroid (papillary, follicular, and mixed cell) all had the recurrent laryngeal nerves exposed in the thyroid space on both sides. None shows permanent paralysis. One patient with a large substernal thyroid has incomplete paralysis on the left side. These patients and all those having had previous thyroid surgery are excluded from this report as they do not conform to routine subtotal thyroidectomy. Also excluded are all patients referred for contemplated extralaryngeal repair for previous laryngeal paralysis. A report on all such cases including all "King operations" performed here by Dr. King or his associates and co-workers (Rosellini, Weber, Gregg, and Hutchinson) for a period of fifteen years is presently being prepared under the direction of Dr. Carl Hutchinson. Dr. Brien T. King has recently retired, leaving his work in vocal cord paralysis to the interest of his associates who have worked with him at the Providence Hospital for the past fifteen years.

SYMPTOMS OF LARYNGEAL PARALYSIS

The symptoms of laryngeal paralysis vary, depending on the type of paralysis sustained—all the way from hoarseness, choking or coughing, and dyspnea with severe night snoring, to suffocation.

From the experimental viewpoint, the following symptoms would be expected in thyroidectomized patients with extralaryngeal nerve paralysis:

Pure bilateral adductor paralysis—	no voice, no respiratory difficulty, no true cough reflex.
Pure bilateral abductor paralysis—	no airway, tracheal collapse, cyanosis, possible death.
Bilateral laryngeal trunk paralysis—	hoarseness, snoring, moderate dyspnea, symptoms increasing with time.
Unilateral adductor paralysis—	poor or weak voice, poor cough reflex.
Unilateral abductor paralysis—	minimal symptoms, no voice changes.
Unilateral laryngeal trunk paralysis—	may be no symptoms unless person is singer or speaker.
Superior laryngeal paralysis—	cough, choking sensation, voice change.

ANATOMICAL STUDIES OF THE RECURRENT LARYNGEAL NERVE

Rustad[6] offers the opinion that dissection of the recurrent laryngeal nerve in thyroid surgery might not be helpful but in fact confusing to the surgeon on the basis that the nerve branches are too numerous to be visualized. Wade's report[7] on a series of 100 patients submitted to subtotal thyroidectomy in which the recurrent laryngeal nerves were dissected out on both sides would give support to a view that the nerves can be observed in their entirety without danger. In fact, strong evidence is submitted to show that such procedure protects against vocal cord paralysis. This report shows 15 per cent of the nerves were in point of vulnerability either in absolute or potential danger, the right more frequently than the left. Eighty-four of the 100 patients were examined before and after surgery and no evidence of immediate or delayed cord dysfunction found despite wide exposure of the nerves at operation.

The number of branches noted in cadaver dissection is more frequently two than any greater number. Review of the literature by Bowden[8] reveals 434 recurrent laryngeal nerves with extralaryn-

geal branches out of 1174 nerves dissected. The site of extralaryngeal division in 300 nerves was divided at or below the lower one-third of the thyroid gland, 133 at the middle one-third and 53 in the space occupied by the upper one-third of the thyroid gland. The greater portion of these nerves divided into two branches. Unbranched nerves were found to enter the larynx in 35 out of 126 subjects.

Table I shows the approximate number of extralaryngeal branches

TABLE I

EXTRALARYNGEAL BRANCHES OF THE RECURRENT LARYNGEAL NERVES

	NUMBER OF NERVES THAT BRANCH
Bowden[8] (1955)	42 out of 54
Rustad[18] (1954)	86 out of 100
Sunderland and Swaney[8] (1952)	91 out of 131
Armstrong and Hinton[19] (1951)	73 out of 100
King and Gregg[2] (1948)	12 out of 43
Weeks and Hinton[11] (1942)	33 out of 41
Berlin[15] (1935)	2 out of 72
Nordland[16] (1930)	2 out of 62
Dilworth[8] (1921)	66 out of 66
	407 out of 669

of the recurrent laryngeal nerves by various reports from 1921 to 1955. Relative relationship of the recurrent laryngeal nerve (disregarding differences between right and left side) to the inferior thyroid artery is shown in Table II.

TABLE II

RELATIONSHIP OF THE RECURRENT LARYNGEAL NERVE TO THE INFERIOR THYROID ARTERY

	NUMBER NERVES	POSTERIOR TO ARTERY	ANTERIOR TO ARTERY	BETWEEN BRANCHES
Bachhuber[20]	200	88	29	83
Berlin[15]	140	75	45	20
Berlin and Lahey[21]	44	22	22	...
Bowden[8]	55	24	11	20
Fowler and Hansen[10]	400	262	104	34
Nordland[16]	62	15	22	24
Rustad[6]	200	93	55	52
Wade[7]	200	85	21	69
Weeks and Hinton[11]	38	18	18	2
Ziegelman[9]	42	12	17	13
	1381	694	344	317

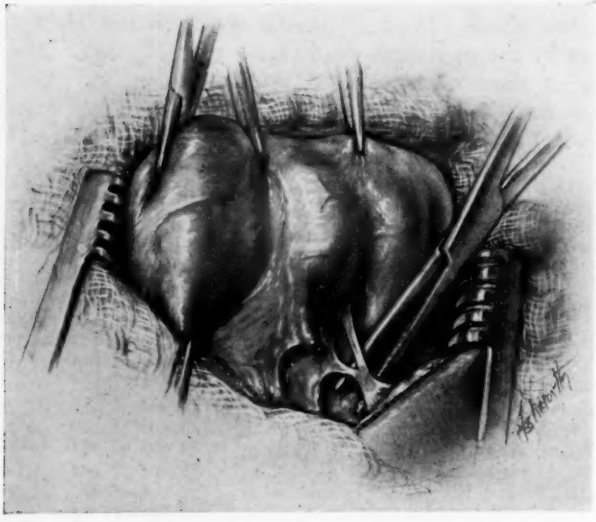


Fig. 13.—Human. Division of recurrent laryngeal nerve into adductor and abductor branches, seen at operation.

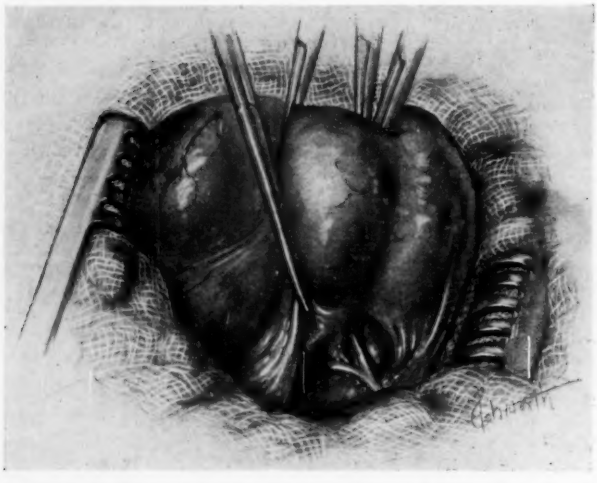


Fig. 14.—Human. Division of recurrent laryngeal nerve into adductor and abductor branches.

Ziegelman[9] pointed out two practical points as regards these relationships, that as a rule the nerve on the left was situated somewhat deeper than on the right, and so better protected; and that the point of contact of the nerve and artery was more frequently behind the middle third of the thyroid gland than at the lower pole of the gland as had been previously stated. The inferior thyroid artery usually enters the thyroid gland on the posterior surface, more near the middle of the gland than at the lower pole. This point has been emphasized many times in the literature but cannot be overemphasized as it represents the point of greatest hazard. An accompanying photograph and illustration show this to be the location of the sutures found on our patients previously mentioned.

HOW LONG DOES PARALYSIS PERSIST WHEN THE RECURRENT LARYNGEAL NERVE IS CLAMPED OR TIED?

The report on experimental laryngeal paralysis[3] did not include that portion of the survey where we attempted to confirm or disprove the previous work of others regarding the susceptibility of the laryngeal nerves to damage.

Although we were unable to produce convincing evidence of just how much injury or damage the nerves can take and still get a subsequent return of function of the laryngeal muscles, we are ourselves perfectly satisfied that these nerves are far from fragile and can withstand considerable handling and pulling. They can be cleaned off, including all branches, without loss of function in the muscle. Also they can be tied off with silk or catgut, and provided these sutures are removed within a few hours, return of function may be noticed in a matter of weeks. Once a nerve was severed or a section removed from it, however, no return of function was ever seen, the affected muscle remained permanently paralyzed.

Return of Function in Two Months. The recurrent laryngeal nerve trunks were crushed by clamping in a hemostat on March 22. One week later the vocal cords were examined and found to be completely paralyzed. No bark was present and coughing was difficult as a gush of air would result at each attempt, and the dog was unable to expel mucus collecting in the trachea. Six weeks passed without return of bark tone. Examination of the vocal cords on May 14 revealed an inability to abduct or adduct either cord. The bark gradually returned and on June 1 the recurrent laryngeal nerves were again isolated and found to be

DIVISION OF RECURRENT LARYNGEAL NERVE INTO ADDUCTOR AND ABDUCTOR BRANCHES

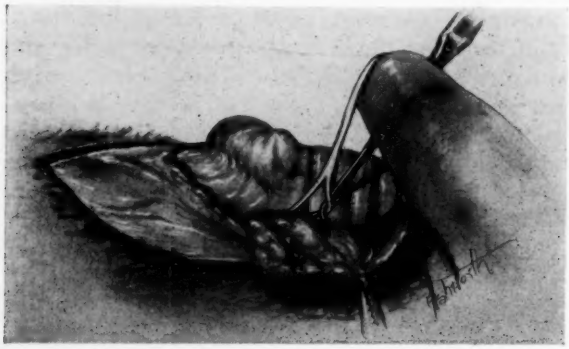


Fig. 15.—Dog No. 22.

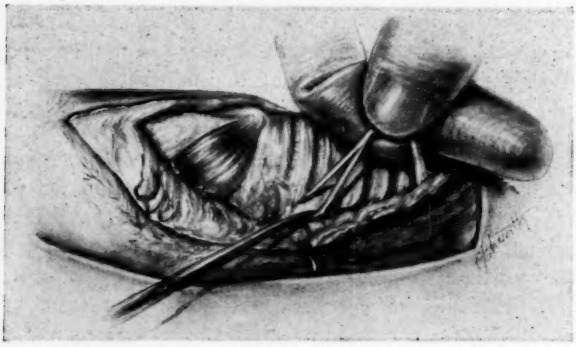


Fig. 16.—Dog No. 3.

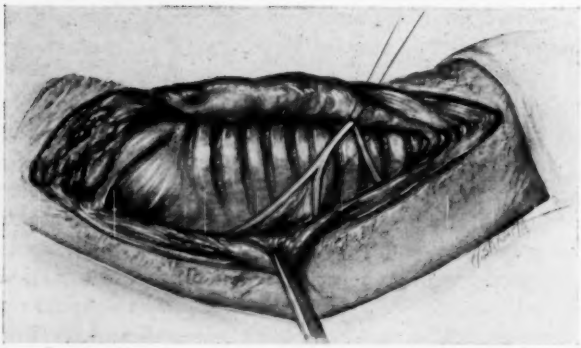


Fig. 17.—Dog No. 10.

normal in appearance. Stimulation of the nerves at any point along the trunk caused closure of the glottis. The action of the vocal cords seemed normal. It took from March 22 to June 1 to fully regain function after crushing the nerve trunks with a hemostat.

Chromic gut No. 0 was then tied firmly on both recurrent nerves of this same dog and left on for two hours. Stimulation of the nerves distal to the tie caused closure of the glottis by adduction of the vocal cords but stimulation proximal to the knot failed to show any response in the larynx. By July 2, the bark was returning, though rough and weak. By July 12, the bark was fully recovered and examination revealed full function of the larynx. It took from June 1 to July 12 to overcome the damage of tying the nerves off for two hours.

No Return of Function After Tying the Nerves for Four Hours. On June 8 and July 19 chromic No. 0 sutures were placed on the recurrent nerves of two other animals, and left on for four hours each. By August 2, both dogs were healthy but totally unable to bark, nor did they regain the ability to bark at all subsequently.

Return of Function After Tying the Nerves for Six Hours. Series II, Dog No. 20. On August 2, chromic ties were placed on both recurrent laryngeal nerves of a very large male hound and left on for six hours.

September 1, bark beginning to return.

September 15, whines a good deal but not barking. No bark on stimulation.

November 29, under nembutal anesthesia, the vocal cords were found to be widely separated. With adequate stimulation, the adductor muscles could bring the vocal cords together.

December 6, still unable to bark.

December 20, re-examination with the dog anesthetized reveals the vocal cords to lie in a midposition. The position of the cords remains unchanged with respiration. The neck was again opened and both recurrent nerves isolated. Electrical stimulation caused the vocal cords to adduct but lacked complete closure of the glottis, an open area remained opposite and between the arytenoid cartilages. Without stimulation directly to the nerves, complete paralysis of both cricoarytenoideus lateralis and posterior was demonstrated.

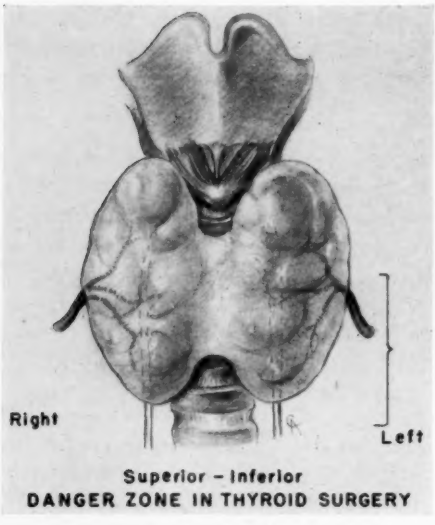


Fig. 18.—Recurrent laryngeal nerves.

The dog had no use of the vocal cords and could not move the arytenoid cartilages with pain stimuli while coming out of the anesthetic.

January 24, the bark is returning. Examination under light intraperitoneal nembutal anesthesia with the laryngoscope reveals full function of the vocal cords, with full and free movement of the arytenoid cartilages. The vocal cords meet in the midline; instantly the dog starts to bark. Full abduction is present with each inspiratory effort. No paralysis can be demonstrated.

Following bilateral suture of the recurrent nerves for a period of six hours, it took from August 2 to January 24 to fully recover function of the larynx, a little over five and a half months.

No Return of Function After Tying the Nerves Fifteen Minutes. Series II, Dog No. 22.

December 3, chromic ties were placed on both recurrent laryngeal nerves of this all-black female dog, and left on for 15 minutes and then removed.

February 3, vocal cords lie fairly well-abducted, intermediate position, and do not respond. No bark present. Paralysis complete. This dog was followed to the next October as the bark did not return at any time.

October 31, examination of the larynx and vocal cords made in surgery. The vocal cords could not be moved to the midline by stimulation nor could movement be induced by efforts of the dog to bark. Complete bilateral recurrent laryngeal nerve trunk paralysis was present. The chromic ties had remained on for only 15 minutes but a permanent paralysis resulted (11 months). The dog was sacrificed and the larynx sent to a pathologist for examination. Report on the slides from the Laboratory of Clinical Medicine revealed, "No evidence of muscle atrophy or degeneration." The arytenoid cartilages were not ankylosed.

We do not have the answer to the question, "Why can one dog survive and recover from paralysis as the result of tying off the recurrent nerves for six hours while another cannot recover the function of the larynx when the nerves are tied off 15 minutes only?"

Although we did not go into this phase of the project in the report made on experimental laryngeal paralysis in 1956, the various types of paralysis were touched upon. A great deal of work remains to be done before we thoroughly understand the variances in response to injury.

SUPERIOR LARYNGEAL NERVE PARALYSIS

Fowler and Hanson,[10] Weeks and Hinton,[11] Frazier and Erb,[12] and Moran and Castro[13] have discussed some complications relative to injury of the superior laryngeal nerve in thyroid surgery. In the past few years considerable attention has been given to the possibility of postsurgical symptoms being related to the injury of these nerves.

The motor branch of the superior laryngeal nerve lies in close relationship to the superior thyroid artery and is exposed to injury in total and subtotal thyroidectomy. When bilateral paralysis of the cricothyroid muscle occurs from injury to these nerves, the patient loses the ability to elevate the anterior border of the cricoid cartilage. Thus it is probable that a certain lowering of tension results in the vocal cords. No simple method, such as laryngeal mirror examination,

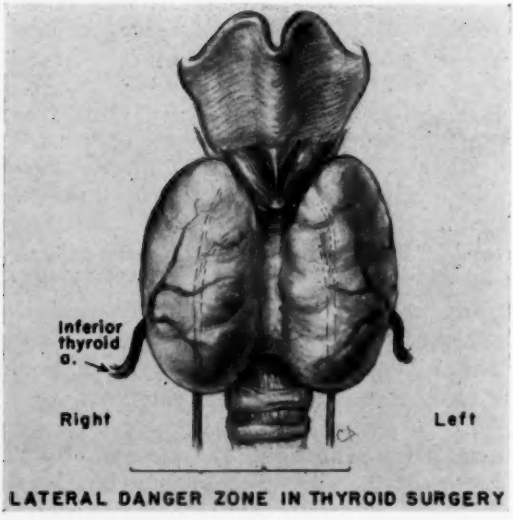


Fig. 19.—Recurrent laryngeal nerves.

can be used to accurately diagnose either unilateral or bilateral superior laryngeal nerve injury.

In spite of examining many hundreds of vocal cords with the laryngeal mirror, it has been impossible to tell whether or not superior laryngeal nerve paralysis is present. It might be possible to use the observations made on the dogs to give a clue in developing visible signs of paralysis in the cricothyroid muscle. If it is possible to stimulate the larynx in such a manner as to activate one normal muscle in this region, a depression may be noticed and palpated on the paralyzed side. The following observations resulted from experiments on the animal larynx:

> Injury to one superior laryngeal nerve with stimulation of the other results in a tortion action of the cricoid cartilage. The normal or unactivated cricothyroid muscle draws the anterior portion of the cricoid cartilage toward the normal side, at the same time the cartilage is elevated. With unilateral paralysis of the cricothyroid muscle, the bark tone is lowered. The bark tone seems affected to a greater degree by unilateral superior laryngeal nerve injury than by bilateral. Injury of the superior laryngeal nerve proximal to the division into motor and sensory branches

results in visible changes in the mucosa of the superior larynx.

Loss of tension of the vocal cords from paralyzed cricothyroid muscles might ruin a singing voice. For this reason, the superior laryngeal nerves should be protected in thyroid surgery of all persons with highly-trained larynxes, as a minimal precaution. Dr. Bowles, associate thyroidologist, contends that the superior laryngeal nerve is injured not infrequently and accounts for the persistent cough encountered postsurgically in these patients. He says that superior laryngeal nerve paralysis must be made on clinical evidence, but that it is far from a rare occurrence.

PROGNOSIS IN LARYNGEAL NERVE PARALYSIS

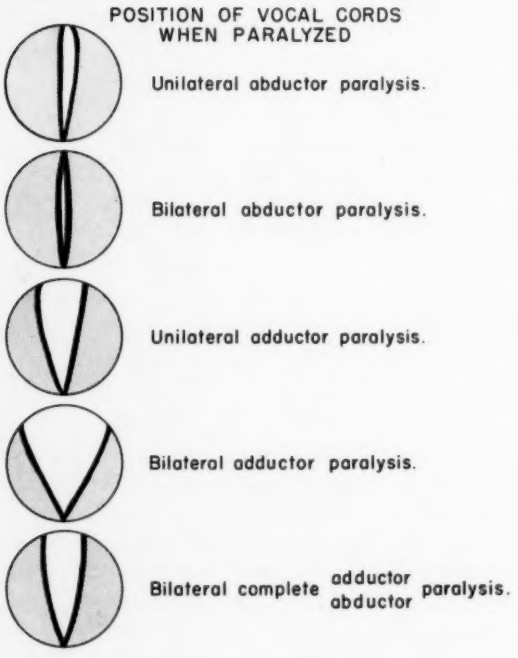
The question frequently arises as to how long a paralysis of the larynx can last without requiring some form of surgical relief. Usually the patient with bilateral recurrent nerve trunk paralysis will seek relief within a few months up to three or four years. Last week Dr. Weber performed a King operation on a patient who was first operated on in 1912. Following thyroidectomy at that time, she experienced symptoms of laryngeal paralysis and was told both vocal cords were paralyzed. Her voice was fairly good but she was unable to do much work. The past few months she has experienced increasing dyspnea to the point recently where she has feared suffocation. Dr. Weber stated that the arytenoid cartilage moved freely, showing no evidence of ankylosis. After the King procedure, her dyspnea was completely relieved and the voice was fair but lower in tone.

IS BILATERAL ABDUCTOR PARALYSIS A MISNOMER?

Most patients diagnosed as having bilateral abductor paralysis actually have bilateral complete recurrent laryngeal nerve trunk paralysis, or more accurately, paralysis of both abductor and both adductor muscles. Pure abductor paralysis is rare and very tragic. It is an immediate surgical emergency.

Pure adductor paralysis is not an emergency but would be just as tragic, as the patient would have no voice as long as this type of paralysis exists.

Recurrent laryngeal nerve trunk paralysis, either unilateral or bilateral, makes up the greatest percentage of cases of laryngeal paralysis and it is for this variety that most patients seek surgical relief. Immediate relief by tracheotomy is accepted by few for a very long time.



PRACTICAL ASPECTS FOR THYROID SURGERY

Rustad,[6] Rustad and Morrison,[14] Berlin,[15] Nordland,[16] Lahey,[17] Fowler and Hansen,[10] King and Gregg,[2] Bowden,[8] Weeks and Hinton,[11] and many others have called attention to extralaryngeal branching of the recurrent nerves. These and other workers have also emphasized the relationship of the recurrent laryngeal nerves to the inferior thyroid artery. Many months of study must have been required by most of these co-workers and certainly a great deal of valuable information has resulted from their continued interest in the problem, and much remains to be done. We do not intend to detract in the least from the importance of this work in our desire to "boil" this information down to meet the practical requirements of the thyroid surgeon in avoiding injury to the nerves. But certain practical aspects must be sought.

In the first place, it does not really matter how often the recurrent nerve passes in front, behind, or between the branches of the

inferior thyroid artery. The important point is that, in the main, the nerve can be found in this location rather readily. Also it does not really matter that the nerves vary a little when the right side is compared to the left. Nor does it concern us too much that the nerve branches within the danger zone of the thyroid space, provided that we recognize this as fact and that we should make an effort to assure visualizing both main branches. The infrequent number of times that the recurrent nerve divides into several branches concerns us rather little, if we injure none of them. On the average, the nerve can be readily found; it remains as one trunk or, at most, two branches, in a high percentage of cases and can be dissected free without too much loss of time or technical difficulty. It is important that the surgeon learning to do thyroidectomy be encouraged to visualize the recurrent nerves.

CONCLUSION

1. Some of the types of vocal cord paralysis produced on dogs have been demonstrated as an aid to explaining what may occur in patients undergoing thyroidectomy. Attention is given to the difference between pure abductor and pure adductor paralysis as well as recurrent laryngeal nerve trunk paralysis. Dissection of the recurrent nerves in dogs is suggested as a further teaching aid in the prevention of vocal cord paralysis.

2. Branching of the recurrent laryngeal nerve does not seem to detract from the value of visualizing the nerve at thyroid surgery.

3. Injury to the extralaryngeal nerves with resulting paralysis to the laryngeal muscles may be temporary or permanent depending on factors as yet not explained. The nerves are neither brittle nor fragile and can withstand considerable handling but the effects of crushing injury are harmful and may be permanent.

4. Visualization of the recurrent laryngeal nerves during thyroid surgery is strongly recommended. After considerable experience with patients requiring the King operation for relief of vocal cord paralysis, we have come to the conclusion that the time and energy required to develop any technique in order to avoid injury to the extralaryngeal nerves is well worth the effort, to patient and surgeon alike.

2244 West 56th St.

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LARYNX, VOICE, ANIMALS AND MAN

PROF. DR. EELCO HUIZINGA
GRONINGEN, NETHERLANDS

I regard it as a great honor and it gives me a very great pleasure to be able to address you here today, and naturally I have asked myself why this privilege should be given to me. I have decided that my being a Dutchman may have had something to do with it. For our chairman—Hans von Leden, who has done such wonderful work in the organizing of this congress—told me that he is of Dutch extraction: the voice of the blood! The name of his family used to be van Leiden, which means that they hailed from Leiden—the city which has played so important a part in the history of my country. Hearing the name Leiden, and being a medical man, one is reminded in the first place of Boerhaave, the greatest clinician and medical teacher of his days. A curious fact about Boerhaave is that, although he never travelled farther than from Leiden to Harderwijk, a distance of some 50 miles, hardly anybody has had a greater influence on medical science throughout the whole world in the course of the past few centuries. He was a professor in the University of Leiden from 1709 to 1738, and during these years 1,919 medical students were registered there, for the most part foreigners. Not less than 659, or more than one-third, were English-speaking. His favorite pupil, van Swieten, was the founder of the famous Viennese school. The well-known medical school of Edinburgh is regarded as a direct continuation of the Leiden school. As we heard from Sigerist of Johns Hopkins, who came over on the occasion of the commemoration of Boerhaave in 1938, the majority of Americans then studying abroad went to Edinburgh. Those were the days of the foundation of the first medical schools in this country, on which Boerhaave has indirectly exerted considerable influence. I have started out with this brief historical introduction because it is useful, at an international congress such as this, to remind us how we belong together.

Here, in Chicago, we have had a gathering for three very successful days of specialists in a variety of different fields, with one interest

Read before the International Voice Conference, Chicago, May 22, 1957.

in common, viz., the larynx and the voice. In numerous countries specialists are today engaged in improving the voice. Much has changed since the days of Sir Morell Mackenzie who, in 1886, complained that the development of the speaking voice could be called a lost art. There is food for thought in the realization that in the ancient civilizations there was a whole nation that was more skilled in this art than we are today. The Greeks were very much aware of the necessity of development of the speaking voice. A well-known example is the trouble to which Demosthenes went to become a good orator. He recited as he climbed hills and walked against a gale on the beach. He trained himself in speaking with pebbles in the mouth. That he originally was a stammerer was probably slander initiated by Plutarch. The Greeks, and later the Romans too, were familiar with the logopedist, whom they called phonascos.

The Greeks had a highly developed sense of hearing; actors who made a mistake of a fraction of a second in the rhythm of reciting the hexameters were immediately hissed. The same holds true probably for the pitch of voice. At one time poor speaking was the immediate cause of a very embittered war.

The time was the year 282 B.C. and the place was a corner of the world where, as we all know, things are unfortunately not always so quiet even today: the Mediterranean. The important Greek colony Tarente was having difficulties with Rome. Roman ships had been destroyed because, ignoring the old treaties, they had entered the bay of Tarente along the promontory south of Kroton. Rome at the time regarded a war as highly inopportune; they sent an ambassador, Lucius Postumus, with very mild conditions. He was received in the amphitheater but the audience repeatedly hissed him down because he was such a poor speaker. Finally his toga was soiled, and he shouted in anger: "This garment will be cleaned with streams of your blood." And he was right, for this was the beginning of years of war against Pyrrhus. If only the Roman Lucius Postumus had had speech correction!

The development of laryngology was made possible by the invention of the laryngeal mirror by Manuel Garcia in September 1854. Garcia was a great singer, founder of the famous school of singers which has produced stars such as Jenny Lind. Garcia was greatly interested in the movements of the vocal cords, and it was in Paris that he suddenly had an inspiration and saw the entire technique in his

mind's eye. He hurried to the well-known instrument-maker, Charrière, took a dental mirror, introduced it, let the sun shine on it and inspected his own vocal cords with the aid of a hand mirror. He reported his discovery in a brief, clear paper to the Royal Society in London in March 1855. He was a very modest man, and he remained silent when, in 1857, the medical world started to use his method, whereafter the unsavory quarrel began between Türck and Czermak about the priority of the invention of the laryngeal mirror. In 1905, however, when Garcia celebrated his 100th anniversary, he was given full homage in London by the laryngologists under the leadership of Sir Felix Semon.

It is surprising that the dental mirror had been used for many centuries before anybody thought of introducing it slightly further for examination of throat and larynx. We have a somewhat similar instance in endoscopy. Kussmaul performed the first esophagoscopy in 1868, but it became generally known only in 1881 after the publication of Mikulicz. Although the tube was sometimes inadvertently inserted into the trachea it was not until 1897 that Killian performed the first bronchoscopy. It is as if during these 16 years a notice had been placed in front of the larynx with the inscription, "entrance forbidden."

It is now a hundred years since the movements of the vocal cords were first inspected with the aid of a mirror. And still there are considerable difficulties in explaining these movements. In the world of the laryngeal physiologists there is today a great controversy between the advocates of the old myoelastic theory, which to many seems so convincing, and the modern trend of Husson's "théorie neurochronaxique." A large number of investigations have fortunately been made as a result. The new theory has in it much that is attractive; I am inclined to find it more romantic, too. There is something rather prosaic in the assumption that the human voice, in which the whole range of human emotions are so clearly expressed and which offers us such a variety of beauty in reciting and singing, is determined exclusively by the subglottic pressure and the mass and tension of the vocal cords. One is only too eager to assume that something more central may be involved. Yet it would seem to me that the old mechanical theory has not yet been disposed of. The controversy will undoubtedly be solved in the years to come, and it may be hoped that this solution will be associated with an improved understanding of the function of the larynx.

As an otolaryngologist I was pleased to hear that the great Congress in Washington, D.C., was followed by the congresses in Philadelphia, St. Louis and Chicago; this makes it clear that these three important branches are still regarded as being within our field. St. Louis and Chicago might be regarded as one entity, because hearing and speaking are a unity which is among the most valuable and certainly the most characteristic possessions of man. It is of great importance that the otolaryngologist improves the standing of our specialty by bearing this fact in mind. Naturally he is a valuable member of the profession if he can perform the correct operations on the mastoid and the larynx; but he raises the level of our specialty if he is also deeply interested in hearing and speaking. Everyone who loves our specialty, therefore, should strive to ensure that these two branches remain closely correlated with otolaryngology. We in Groningen, as in many other places, are fortunate in having both the audiological department (Prof. Huizing) and the logopedic department (Mrs. Moolenaar-Bijl) within the otolaryngological clinic. For all of us it is a good thing to be under the same roof; it has led to a co-operation which has been very satisfactory and beneficial to all parties concerned.

The everyday work of the laryngologist is done at a vital point. The intersection of the trachea and the esophagus has become so important in medicine that a large number of specialists have in the past few years gathered round this point; even a certain degree of crowding has been noticed! The time may come when the laryngologist will have to start directing traffic at this point. But, however pleasantly various specialists will be permitted to pass through and by the larynx, the physiology and pathology of the larynx will remain our undisputed field.

Phylogenetically, the oldest function of the larynx is its function as a sphincter, which separates the air passage from the digestive tract. This has always been, naturally, its most important function also in man. But the function as an organ of speech has been of infinitely greater importance for the evolution of mankind. In this development the contact with fellow-men has principally been made through the medium of the organs of speech and hearing. Contact may very well have been obtained in some other form, but almost certainly with a less favorable result and the origin of an even less perfect man. Vision is doubtless also important, but less important than the spoken word, as far as human interrelations and especially the development

of mankind are concerned. Probably no author has stated it more clearly than Wells in an utopian novel. Suppose that all our ancestors had been blinded early in the history of mankind. Quite apart from serious difficulties in the struggle for life as a result of this severe invalidity it might none the less be presumed that mankind would have been capable of some degree of further development. But such further development would certainly have been impossible had our ancestors been completely deaf. And the tactile sense—well, in contrast with ants, it is used by man only on particularly intimate occasions.

Other insects maintain already an unmistakable contact based on the interaction between sound production and hearing—an interaction which is extremely important to the species. Interesting experiments have been made in this country with grasshoppers, whose auditory organ shows a fairly high degree of development. A male grasshopper was placed in front of a microphone as he produced his high-pitched sounds. Another grasshopper, placed near a loudspeaker many miles from the microphone, was greatly excited by the chirping. I need hardly tell you that the latter grasshopper was a female.

The grasshopper produces the high-pitched sound with the aid of what might be called a rasp on his wings. Just imagine man producing his sounds in the same way—he would only need to move his arms. How much less interesting it would be to follow a speech delivered in this way. The vividness of human contact is mainly determined by the important intersection which I have just mentioned. This intersection provides a possibility of aspiration to which mankind has often paid heavy toll. But on the other hand there is the great advantage of our speech becoming much more lively because it makes use of muscles originally designed for the intake of food. Facial expression and tone of speech are mutually adjusted. This may have been very useful in the development of communication on a higher plane.

The information theory has again drawn attention to the great significance of communications between man and his fellow-man. Our entire society is determined by this communication. What is communication? This is apparently not at all easy to define. Stevens gives the following definition: "Communication is the discriminatory response of an organism to a stimulus." This definition shows marked behavioristic features. It offers the advantage of including both man

and animals, for naturally information is of the utmost importance to animals, too. In spite of its generality, arguments can be found even against this definition.

Numerous investigations have been made in the past few years into communication among animals. Roth in this country investigated the love life of the mosquito. The male mosquito is active in this respect, whereas the larger female is purely passive. The mosquito perceives sound vibrations by means of the tactile sense, localized in the antennae. The male mosquito responds to sound frequencies of 100-800 vibrations per second, but its sensitivity to vibrations is by far the most acute for frequencies in the 250-500 range. This corresponds to the sound produced by a grown female when flying; it is the well-known buzzing sound which is so irritating to the human ear. And it is exclusively this sound that constitutes the stimulus to the male mosquito; smell or vision are of no importance whatever in this respect. A male may land in the immediate vicinity of a resting female, without showing the least sign of interest. But hardly is the female airborne than the male becomes all active and lovelorn. This may be repeated an incredible number of times, for a male mosquito is a true Casanova. This sound stimulus is of paramount importance to mosquitoes because it is only by virtue of this sound that the species is continued. This procedure may certainly be called communication in the sense introduced by Stevens. There is a stimulus, produced by the female, followed by a response on the part of the male, the significance of which one could hardly fail to recognize. But if a tuning fork of the same frequency as the wingbeat of the female is used, then all males are immediately enamored of the tuning fork: the response is completely identical with the response to the flying female. Yet many of us would no doubt seriously object to this being described as a communication between a tuning fork and a mosquito!

This experiment clearly illustrates the low level at which the communication is accomplished in this case. The objection may be made that these were "only mosquitos," but animals of a higher order, too, have never reached a much higher level in this respect. Yet animals sometimes obtain information in a manner which makes the human sensory function look downright deficient by comparison. Mention need only be made, in this respect, of the olfactory sense in many animal species, and of the bat, which is able to perceive frequencies up to 90,000 vibrations per second and which as a result is capable of what may be called radar-guided flight.

Man gets most information through the voice of his fellow-men. Human speech, like writing, is a code, and as such well suited to mathematical calculations. This is the basis of the information theory. The salient fact in man is that the information, expressed in code, is understood and gives rise to a train of thoughts which, converted into code, can be sent out again as new information.

Some of the "intelligent" animals have shown some rudimentary development of speech resulting from the company of man. The results of many centuries of close association can be roughly estimated at a degree of development which does not exceed that seen in a child aged 18 months. But no animal alone has ever reached this level; this can only be achieved by combining two animals.

Speech development in man starts at the age of three to six months, during what is known as the bubbling period. Two factors are of great importance here: the child feels a mysterious urge to produce sound, and attempts to imitate as best it can. It imitates the sounds of its environment, and soon gibbers words in imitation of the enchanted relatives. It improves these words, thanks to an auditory control, thus producing a typical example of "feed back." An 18-month-old child has a passive vocabulary in that it understands short sentences such as: "How tall is Johnny?" and "How glad is Johnny?" But any dog is capable of the same understanding: "Coming for a walk?" or "Go find the master." Bühler calls this "Lautdressur." The child, in addition, has an active vocabulary and produces short sentences. But so does a parrot. A child of one and one-half years is thus a dog plus a parrot. Then the child shows a breakthrough which is of very great importance: it understands that, with a certain word, something can be indicated. So communication develops at a level that is characteristic of mankind.

There are a great many tall stories about parrots but they are either pure fantasy or they relate to a parrot which by chance happened to produce one of its standard sentences at an appropriate moment, usually creating a comic situation. The best parrot story I know hails from Groningen. Once upon a time there was a grocer who had a parrot and a dog. One afternoon the coal-vendor happened to pass the shop, which at that moment was empty. He shouted through the open door: "Do you want any coke?," and the parrot immediately replied: "Yes, bring 20 hundredweight tomorrow." When the coke was delivered, customers crowded the shop and the grocer,

harassed as he was, was furious. Who ordered coke? Nobody knows. Of course, the parrot was blamed, and was consequently kicked under the counter. A moment later one of the better customers trips over the dog, which is likewise kicked under the counter. Whereupon suddenly the parrot's voice says: "Did you order coke, too?"

Again I have been unable to resist the temptation to tell this old joke from my home town, because actually it involves something very essential. If this situation had been real, then there would be no difference in this respect between man and animal. A parrot is obviously capable of correlating a word and an event. It is also capable of prompting its keeper by means of certain movements. It might then be expected that the animal might be able to correlate word and object, but strangely enough this is not so. Koehler, who obtained remarkable results in scientific bird-training, tried to train a talented parrot so as to make it say "eat" when it was hungry and "water" when it was thirsty. He failed, and nobody has so far succeeded. The parrot's brain is incapable of this correlation.

Considerable efforts have often been made to teach higher animals to speak, but all attempts have failed. One chimpanzee is alleged to have been able to say "papa" after two years of careful training, but then the chimpanzee died. Well, you all have probably reached the saturation point as regards animal stories by now. Yet these stories are extremely important. Animals have no speech and will never understand a syllable of our speech. Although this has been an axiom for many centuries, which has been very definitely stated already by such men as Descartes, it appears that many biologists and animal lovers find it difficult to accept this. Yet there is no other way in which the difference between man and animal has been made so clear.

Speech is characteristic of man. Suppose that some day—it is a supposition more hypothetic than real—ape-like beings will be encountered which bear a very nice long tail but nevertheless maintain a lively mutual contact by means of a code, by voice sounds which clearly bear the traces of the symbols of speech. In that case, however painful it may be to be thus confronted with our ancestry, we should have to accept these beings as our fellow-men. And we would undoubtedly soon be engaged in conversation with them.

I shall not dwell on the origin of speech. On this subject there is a comprehensive and often fascinating literature, with an abundance

of theories from many quarters, which would only too easily confuse us. It is all so long ago, probably a few hundreds of thousands of years. But anyone who has studied this literature must of necessity reach the conclusion that not only is speech characteristic of man, but it has also been the factor to which mankind owes its very existence. From an anthropological point of view, *homo sapiens* cannot be imagined to be anything but a speaking and thinking being. In his well-known paper on the origin of speech, Renan writes: "C'est donc un rêve d'imaginer un premier état où l'homme ne parla pas, suivi d'un autre état où il conquit l'usage de la parole." But, before him, as early as 1820, this was even more sharply defined in W. von Humboldt's saying: "Der Mensch ist nur Mensch durch die Sprache."

The beginning of mankind has been correlated by many scholars with the invention of the first tool. But in my opinion Révèsz and others are correct when they maintain that a tool can be devised only when one is conscious of its object; this presupposes the presence of thoughts, which can only have arisen due to the development of speech.

Man's secret lies in the fact that he has been capable of using his voice for the development of speech. Attention has again been drawn to this fact by the information theory, which has been developed as a result of the pioneer work done in this country by Shannon and Wiener.

The information theory was originally a purely mathematical theory, which was not concerned with information as such but with the signs or symbols in which it is expressed, i.e. with the physical representation which lends itself to statistical calculations. At present the scope of the theory is much wider, however, and far more interesting to the otolaryngologist who is concerned with speech and hearing. Hallowell Davis has stated that the information theory will assume as great an importance in biology and psychology as the quantum and the relativity theory together have done for the exact sciences. Some even expect to find here the key to the mystery of the relation between the mind and the body. However, the only established fact for the time being is that information and entropy can be calculated by statistical methods in a similar manner, and that information equals negative entropy.

The world is gradually evolving towards a condition of the greatest possible disorder. This statement is completely innocent of

any political conviction. It is nothing but a gloomy synopsis of the second major law of nature which, expressed in more scientific terms, states: the world's entropy is ever increasing. All physical and chemical processes are determined by two major laws. The first law concerns the preservation of energy. The second determines the direction in which these processes develop. The conception of entropy was introduced by Clausius as early as the middle of the last century. This brings the formulation: the entropy for a certain system increases or, at best, remains constant. Nature intends to deprive energy of its value by levelling the differences. Boltzmann observed that the entropy of a certain system is characterized as the probability of its condition. The various systems in general are always assuming a condition of increasing probability, and entropy consequently increases.

The law of entropy will ultimately make life impossible after many millions of years unless man finds the way to a breakthrough in this respect. It is understandable that great significance has been attached to the observation that information equals negative entropy. This is important and this is new. But certainly not new are the more or less philosophical considerations regarding the connection between entropy and vital processes. Entropy was already a subject of considerable discussion in the past century. Ectropy was then introduced as the opposite of entropy; it is a curious fact that this word ectropy is completely obsolete now. The first to point out a possible correlation between vital processes and ectropy was no less an authority than von Helmholtz. His views were subsequently elaborated by Auerbach, who pointed out that it is chiefly the mental processes which are assumed to have an ectropic nature. This theory has subsequently had many advocates. It seems to me that these classical publications are almost forgotten in modern literature.

We now know that information alters the probability condition of a system: the entropy diminishes. There is, consequently, order. It can be stated with certainty that something is put in order in the human brain as soon as man receives information. But does this knowledge bring us much farther? And what precisely is being put in order? Much can be expected to be learned in the future from electrophysiology and pathology of the brain, in which fields such remarkable results have been obtained in the past few years. But will we ever be capable of fathoming the correlation between the body and the mind? Naturally man is ever making progress but one is

nevertheless reminded of Goethe's beautiful words: "Der Mensch muss bei dem Glauben verharren, dass das Unbegreifliche begreiflich sei, er würde sonst nicht forschen."

A particularly striking thought about man and information has been offered by Young. He developed it after having seen and admired Notre Dame in Paris for the first time. Man possesses a mysterious longing to impart information to his fellow-men. Perhaps this explains why some of us become professors. Young correctly points out that modern man has an abundance of easy possibilities of communication; space, too, no longer constitutes a problem. In former days this was quite different, and the space to which man had access was extremely limited. Yet information was imparted to posterity in that monuments were erected, which today still compel our surprised admiration; this was information in time. Following this line of thought, the ancient tumuli and the splendid cathedrals of the Middle Ages can be compared with the ready-made intercontinental communications characteristic of our generation.

It is probably also this mysterious longing to impart and receive information which caused us to gather here in Chicago. We have learned a great deal on this occasion. It might be possible to calculate the number of bits of information received by the attentive listener. Although this is important, there is still something else. But before I touch upon this, I feel that I must apologize for this somewhat fragmentary discourse on a subject about which so much has already been written and to which the greatest thinkers that mankind could produce have devoted themselves. However, there is still one thing which I want to bring up. There is a great contrast between man and animal, because man has undergone an extremely great evolution in the course of the past hundred thousand years. Thanks to the power of speech, man received information different from that received by animals. And it is here that information suddenly becomes a conception of a subtlety far beyond that which can be expressed in mathematical formulae. It is probably to this that Davis alludes when he speaks of information as planning—as action directed at a goal—and as something which he regards as a component in the universe which equals mass and energy in importance. It is on this basis that one can believe in the possibility of a better humanity.

These international congresses are important also because they are a contribution towards an improvement in interhuman relations. I might add, particularly when one is received as heartily as we have

been received here in Chicago. Considering this, is not the choice of this subject an obvious one? For the beginning of interhuman relations originates in the voice.

ACADEMISCH ZIEKENHUIS

LI

VESTIBULAR SENSATION AND THE CEREBRAL CORTEX

WILDER PENFIELD, M.D.

MONTREAL, CANADA

For some years I have made detailed records of our observations of the human cerebral cortex during craniotomies carried out under local anesthesia. The number of such operations is now well over 700 and in general it may be said that about half of the patients thus operated upon were cured of focal epilepsy. I shall say no more about the clinical problems.

It has been demonstrated for laboratory mammals that there is a pathway for projected impulses from the vestibular labyrinth to the cerebral cortex. The vestibular area in the cortex has thus been shown to be adjacent to the auditory area. Gerebtzoff[2] suggested that the vestibulocerebral pathway passed upward in the posterior longitudinal bundle of the ipsilateral side. Mickle and Ades,[4] also Andersson and Gernandt,[1] considered the connection of labyrinth with cerebral cortex to be largely contralateral. From the labyrinth to the cortex is a long jump in terms of physiology. In between come the labyrinthine reflexes. I shall try to make my talk as simple as possible, hoping that we may discover the probable role of the cortex in the utilization of vestibular information.

The labyrinthine reflexes depend upon the brain stem. If one transects the brain stem of the laboratory mammal, through the upper portion of the midbrain, those postural reflexes remain as they were described by Magnus and de Kleijn, by McNally and others. You have then, in a high decerebrate preparation, almost intact the conjugate movements of the eyes and postural reflexes. When the transection is made at a lower level in the midbrain and pons, the reflexes become poor and disappear.

In the fish and lower animals, the old brain, which corresponds with the human brain stem of man, as shown in Figure 1, carries out

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute. Read by invitation before the annual meeting of the American Otological Society May 11, 1956.

the work of neuronal integration. But as the evolutionary scale is ascended the cerebral cortex appears. It is drawn in diagram for man in Figure 1. It would seem that certain functions which had been, let us say, supervised in the old brain in a rudimentary fashion, require a further elaboration. This elaboration is made possible by the appearance of areas of cortex. But the new areas, like lily pads, are connected by a stem with the old subcortical center. Thus the new cortical area increases the possibility and the complexity of the function of the older center.

The older center does not forfeit its function of supervision. The cerebral cortex of man is not "the top." It is an elaboration that makes things possible but it is not the place where final integration takes place. It is not what Hughlings Jackson called the highest level. That remains in the higher brain stem (Fig. 1) in what may be called the central integrating system, the centrencephalic system. Thus the areas of the cortex in both hemispheres are utilized with the brain stem in many of the processes which make consciousness possible. Any interference with the diencephalon and midbrain seems to abolish consciousness. During conscious processes this integrating area is employed together with whatever portions of the cortex are required.

Now, the auditory area of cortex, as has been quite well demonstrated, seems to be located in the transverse gyrus of Heschl (Fig. 2). If you follow the central fissure down, the beginning of Heschl's gyrus is just posterior in its lower end in the superior temporal convolution. It runs inward in the lateral fissure posterior to the insula. The visual area of cortex is in the occipital lobe and somatic sensation has its principal representation in the postcentral gyrus. But there is a second sensory area (somatic) that extends down into the Sylvian fissure. See Figure 2.

Walzl and Mountcastle[6] showed in laboratory animals that evoked potentials from the stimulation of the labyrinth could be recorded in the cerebral cortex between the auditory area, the Rolandic somatic sensory area, and the second somatic sensory area. It is difficult to pass from animal localization to man, by extrapolation, and I shall not attempt it. Instead I will present direct evidence as far as it goes.

Stimulation of the cerebral cortex of conscious patients, during exploratory craniotomy, has occasionally confirmed the findings of the experimentalists. When the records were reviewed in a series of 108 explorations of the temporal lobe, with this in mind, seven patients

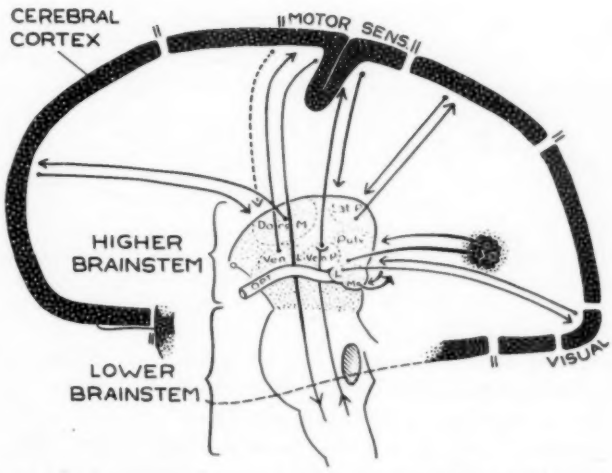

Fig. 1.—Diagrammatic representation of relationship of the human cerebral cortex with the higher brain stem in which important integrative processes must take place. Such central integration makes possible co-ordinated use of both hemispheres. (From Penfield, Comptes Rendus, Congrès Neurologique Internationale, Vol. 3, 1949)

were found to have reported what might be called labyrinthine sensations during the cortical stimulation (Penfield and Jasper, 1954). In this series of 108 cases only temporal and central areas were exposed and stimulated. The findings in operations that exposed other areas of the cortex will be discussed below. Application of a gentle electrical current to the cortex, adjacent to the transverse gyrus of Heschl, produced a dizziness which is best judged by the patients' own words:

Figure 3 shows that all of these points of stimulation fell on the first temporal convolution of one side or the other. The auditory convolution is just deep to this. The patients' own description is reported in the legend to that figure. Hécaen reviewed a large number of our operative records and reached the same conclusion as to a localization of vestibular sensations in the posterior superior temporal region. (See Figure 22, Hécaen, Penfield, Bertrand and Malmo, 1956.)

For the sake of comparison the points of stimulation which produced auditory responses in the same series of cases are shown in Figure 4 and some of those responses in the words of the patient, are described in the legend of that figure.

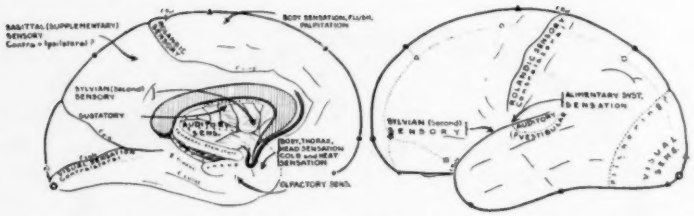

Fig. 2.—Summary of areas of sensory response to stimulation of the human cerebral cortex. Placement of the vestibular sensation next to auditory sensation is only tentative. (From Penfield and Jasper, 1954)

So much for stimulations in the temporal lobe. Electrical stimulation in the parietal lobe may at times result in a sense of rotation or bodily displacement, and seizure discharge here may produce an epileptic aura of that type. I have never reviewed these cases completely but my impression is that such a phenomenon is apt to appear as the result of stimulation or discharge in the posterior mesial portion of the parietal lobe.

Stimulation just anterior to, or even in, the occipital cortex, may cause conjugate deviation of the eyes to the opposite side and, with it, dizziness perhaps, as in the following case:

REPORT OF A CASE

Case B.W. Stimulation in the middle zone of the left occipital lobe (Vis. in Fig. 3) caused this patient to have the usual visual sensation. She saw a light that appeared first in front of her and moved over to the right. Her eyes moved to the right but there was no dizziness. Stimulation more anteriorly (Vert. in Fig. 3) near the frontier between occipital and parietal cortex, caused her to have vertigo. She cried out that everything was moving, turning around. She described the turning as clockwise. Her eyes were seen to deviate to the right and there was nystagmoid jerking of eyes and flickering of eyelids. These movements continued after cessation of the stimulation and the experience resembled, she said, her habitual seizures.

We must ask ourselves whether such phenomena bear any necessary relationship to the vestibular system. One might think so, since overactivity of one labyrinth may produce conjugate deviation of the eyes and nystagmus, as well as a sense of bodily movement or rotation.

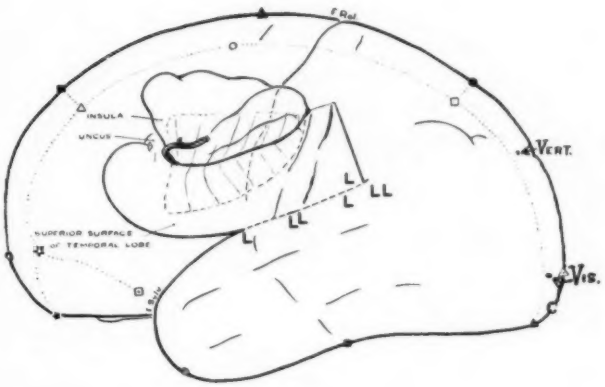

Fig. 3.—Labyrinthine responses which occurred in a series of 108 temporal explorations. The letter 'L' indicates a point where threshold stimulation produces such a sensation. The patients' descriptions follow: Case 5—sinking feeling and sensation of full head; 25—head rest seems to be jumping up and down; 47—"a dizziness all over"; 67—"etourdi" things turning around, whirling; 72—dizziness; 77—moving around; 94—dizziness, swinging, spinning. (From Penfield and Jasper, 1954)

But all of these phenomena make their appearance from time to time as the result of local epileptic discharge or electrical stimulation in different areas of the cortex. A local cortical discharge in almost any area of one cerebral cortex may, as it spread, result in conjugate deviation of the eyes to the opposite side and perhaps turning of the head to that side. It seems likely that a common subcortical mechanism is reached thus from many areas in the cortex.

There, however, are three areas in which local electrical stimulation may cause the eyes to turn to the opposite side most easily. Sherrington pointed out the frontal eye turning area in chimpanzees. It is the same for man but has moved back closer to, and on, the precentral motor strip (Fig. 5). He described turning also from stimulation of the occipital cortex in chimpanzees. We get that result from the occipital cortex for man, too, as from point "Vis" in the case of B.W. just described, but often the conscious patient seems to be looking at the lights and colors which the stimulus produces and so we cannot say that the movement is anything but voluntary. Eye turning without visual sensation occurs more anteriorly as at "Vert."

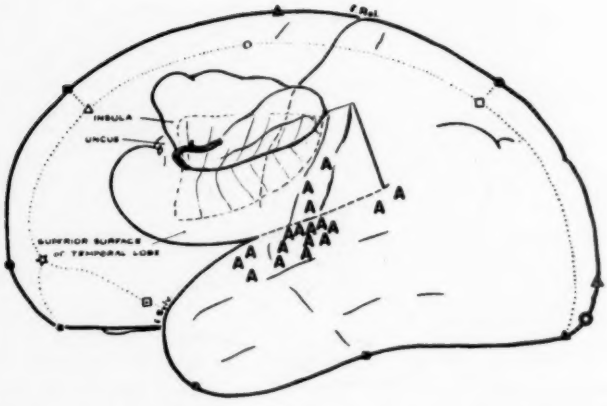

Fig. 4.—Auditory responses to electrical stimulation in 108 temporal explorations, right and left. The superior surface of the temporal lobe and insula are turned upward. The letter 'A' indicates general position of one or more stimulator placements in each case.

Positive responses were described as follows: Case 10—deep tone bell heard in opposite ear; 19—burring sound; 25—two motors "boom, boom, boom"; 32—sounds seem different; 33—"can't hear"; 34—hard to hear; 38—ringing; 57—sound like bird or cricket, voices altered; 66—sound like under water; 60—"un bourdonnement," louder in contralateral ear; 65—buzzing; 67—"deaf a little"; 69—operator's voice changed, ringing; 70—couldn't hear out of opposite ear; 78—"birds chirping"; 84—motor running; 95—operator's voice suddenly distant. (From Penfield and Jasper, 1954)

Eye turning is also produced by stimulation in the supplementary motor area and the head turns in a contraversive looking movement while the opposite hand may be raised as though the patient were looking at what the hand would do.

I believe that nystagmus may occur, occasionally, during such turning of the eyes but we have made no careful analysis of its frequency.

Dizziness is a word patients use not infrequently to describe the effect of stimulation. It is often associated with eye movement or pupillary change. But it occurs in so many areas of the cortex that I could never be sure that it was related to vestibular sensation. Even in those cases of dizziness from stimulation in the temporal lobe which are summarized in Figure 3, I only assume that we are dealing with the direct sensory connection from the vestibular system because of the evidence from animal experimentation.

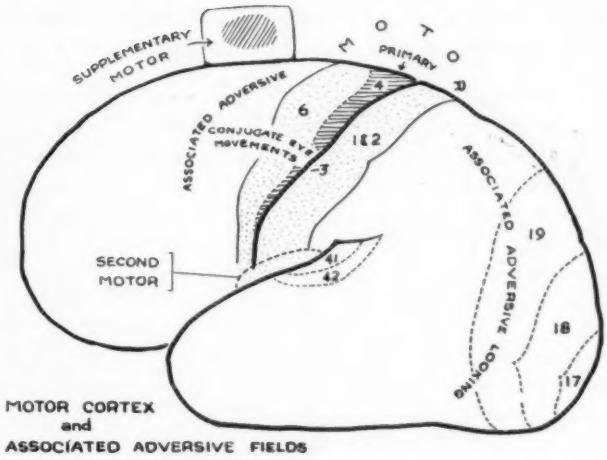

Fig. 5.—Motor areas of the human cortex. Conjugate looking movements of eyes, contraversive, most easily produced: 1) midprecentral gyrus extending forward somewhat on adjacent gyrus. 2) anterior occipital or posterior parietal area. 3) supplementary motor area.

It was never important in the treatment of the patient to put these questions to the test and so no special methods of proving the relationship of such sensation to the labyrinth were tried. Craniotomy under local anesthesia is a therapeutic procedure, not an experimental one, unless experiment offers the patient some advantage. Thus it is that many questions remain unanswered. The time is not far off, however, when the vestibular afferents will be mapped out by evoked potential technique in man. Indeed the technical equipment is fully prepared. It only awaits reasonable opportunity.

It may be of interest to consider what physiological purpose information from the utricle and semicircular canals might serve in the cerebral cortex. Consider for a moment each of the other streams of sensory impulses.

The pain pathway, arising in the periphery, passes up to the thalamus and stops there, without any important detour to the cortex. Discriminative sensation however, arising in the skin, muscles and joints, follows its course to a ganglionic interruption in the lateral nucleus of the thalamus and then passes on to the central convolutions of the cortex. From the cortex it must pass inward again to the

centrencephalic system to be integrated with other streams of input. In a similar way the stream of visual and auditory impulses each makes an important detour out to the cortex and back to brain stem.

My tentative conclusion is that the pathway of vestibular sensory information makes a detour from thalamus out to cortex where the vestibular area is next to the auditory area in the superior temporal convolution of both sides. From there the pathway probably returns to the higher brain stem where it enters the centrencephalic integrating system. Removals of the superior temporal convolution on either side is followed by no defect of vestibular function that we have been able to discover as yet. The same may be said of auditory acuity.

The information might well be utilized during the voluntary employment of the eyes in conjugate movement. It might provide information of importance in the conscious spatial orientation of the body in space, a function in which the temporo-parietal cortex is active particularly in the minor (non-dominant) hemisphere.

NEUROLOGICAL INSTITUTE

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LII

COLLAGEN DISORDERS OF THE RESPIRATORY TRACT

SIR VICTOR NEGUS

LONDON, ENGLAND

In postmortem examination of patients dying during or soon after an asthmatic attack, there has been noticed thickening of the basement membrane of the bronchial mucosa.[2] The process appears to be partially reversible, the layer being less obvious in material obtained between attacks (Figs. 1a and b). There is, however, gradual hypertrophy, time and repeated attacks being necessary for development of the thickened basement membrane "as one would expect from the partly collagenous nature of the thickening."[2] The activity of asthma is roughly assessed by the degree of eosinophil infiltration and thickening of the basement membrane.[2] Also, in systemic scleroderma, according to Talbot,[7] "many small alveoli are surrounded by dense zones of fibrous tissue." "In other areas the alveoli are dilated and contain fragmented alveolar septa, and in many of the smaller bronchi the muscular coat is replaced by fibrous tissue. The bronchioles may be dilated and the walls infiltrated with lymphocytes and plasmocytes." Further, microscopic changes of chronic interstitial pneumonitis with atelectasis are also found in the lungs of patients with systemic lupus erythematosis. Collagen fibers are always present in normal animal lungs and have been well demonstrated by Causey[3] by means of electron microscopy (Fig. 2).

Increase or swelling of collagen will lessen the powers of dilatation and contraction of bronchi, bronchioles and alveoli, sometimes to a permanent degree, with emphysema and difficulty in respiration, as evidenced by asthma.

Not only may increase of collagen fibers interfere permanently with respiration, but there may also be temporary and reversible effects due to temporary swelling of the fibers.

Now collagen fibers, formed of bundles of small fibrils, are elastic and very flexible, but resistant to force; the fibrils are com-

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Read as a discussion, in a symposium on collagen disorders, before the Sixth International Congress of Otolaryngology, Washington, D. C., May 1957.

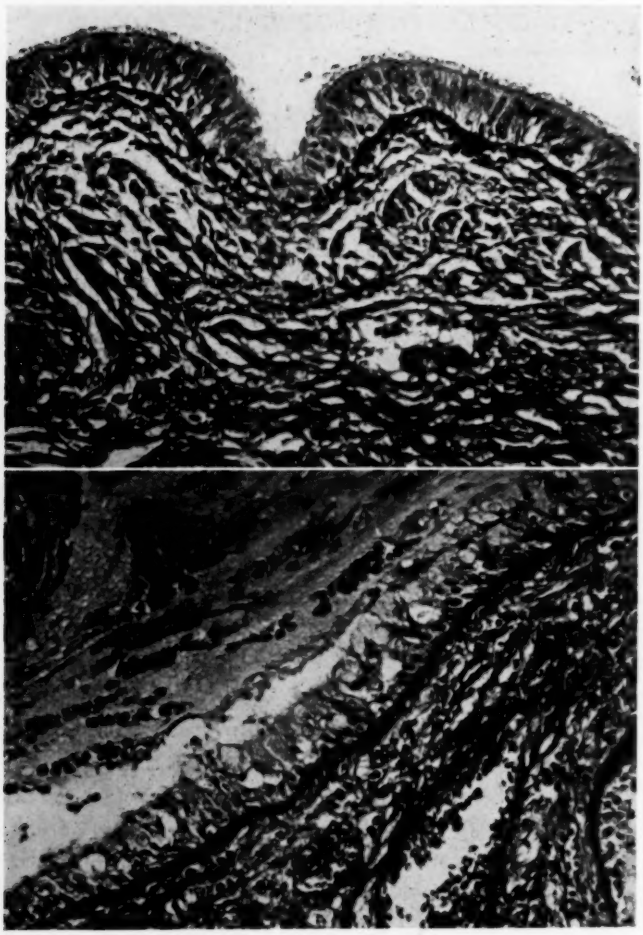

Fig. 1*A*.—Normal small bronchus with cilia and few goblet cells. Basement membrane thin. *B*.—Bronchus from case of asthma with great increase of goblet cells. Reduction of ciliated epithelium and thickening of basement membrane. Stained for collagen with Van Gieson.

Fig. 2.—Electron photomicrograph showing capillaries (cap.), section of red blood corpuscles (RBC), with thin wall separating it from alveolus (alv.) Endothelial cell nucleus is seen (EN.) and scattered collagen fibres (Coll.).

posed of long chain polypeptides,[1a] serving as supporting strands in the intercellular spaces, in a mucopolysaccharide matrix[4] and bathed by tissue fluid with its contained ground substance.[1b] The formation of intercellular collagenous substance is preceded by the appearance of mucopolysaccharides for which vitamin C is essential.[5]

Collagen has an extraordinary faculty of swelling by absorption of water; in pure water the fibers may increase by about 50 per cent in thickness, while in dilute acids or alkalies there is a gain of as much as 4,500 per cent.[4]

The relation of these histological and physiological observations to abnormal changes in the mucosa will be considered mainly in respect of swelling of collagen.

It is recognized that in nasal allergic states the pH of the tissue fluids rises to as high a level as 8.5; presumably similar changes must

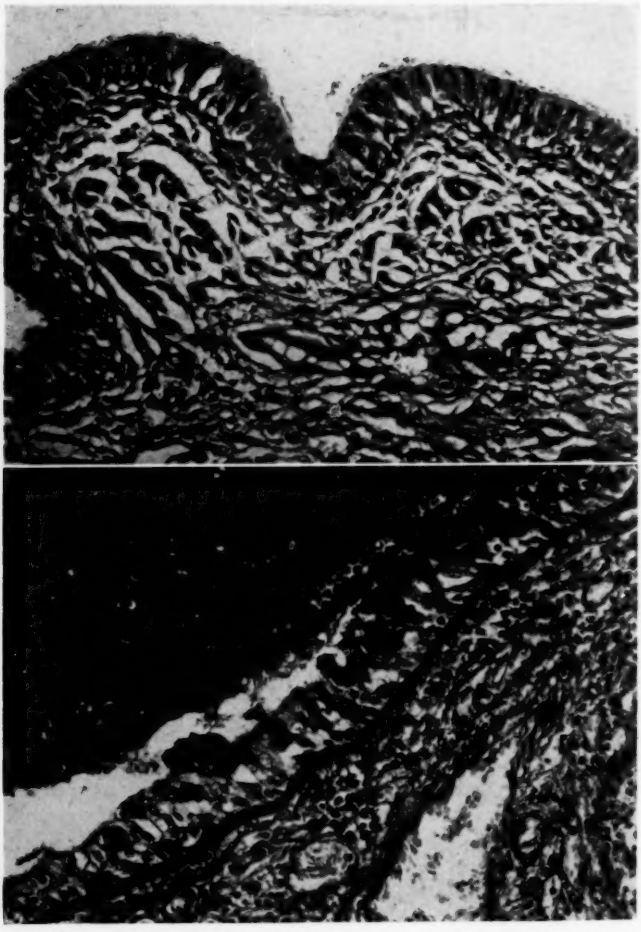

Fig. 3*A*.—Normal bronchus stained with periodic acid Schiff (PAS). *B*.—Bronchus of asthmatic patient with great increase of goblet cells, containing mucus which is stained. Much mucus is seen cast off in the lumen. The basement membrane is thickened.

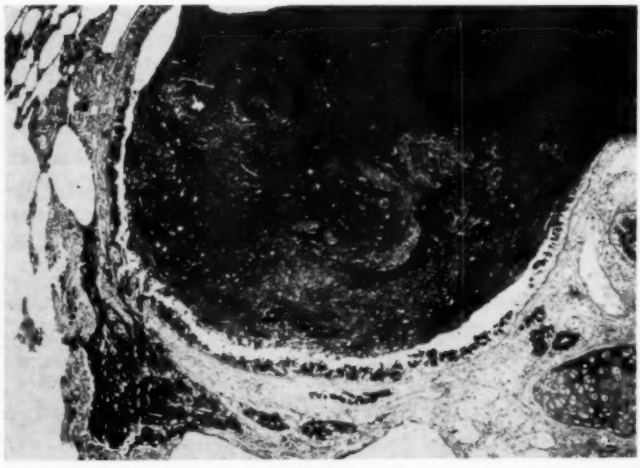

Fig. 4.—Mucus blocking lumen of bronchus. Ciliated epithelium lost in places.

occur in the bronchial tissues. There is, as a result, increased permeability of cell walls with an increase in the intracellular fluid and also in the intercellular fluid, which bathes the collagen fibers. The result of this gain in amount, associated with a rise on the alkaline side, will show itself in swelling of collagen fibers during asthmatic attacks; narrowing of the lumen of the bronchioles and bronchi due to edema of the mucosa, together with the resistance of the swollen collagen fibers to expansion and contraction during respiration, will result in dyspnea. Permanent hypertrophic increase of collagen may be associated with inflammatory changes and aggravation of symptoms and signs, with resultant emphysema and other signs of obstruction.

It is suggested that an ill directed effort at correction of increased permeability is attempted by increased over-production of mucus from numerous newly formed, metaplastic goblet cells and existing racemose glands (Fig. 3a and b). A layer of mucus is recognized as having a waterproofing function in the skin of some fish such as eels and in some amphibia; the hypothesis suggested here is that mucus has a similar action in the respiratory and alimentary tracts, in addition to its other function of avoiding bacterial and virus invasion.

The attempt at repair fails for two reasons; first it is in the tissues themselves that the damage to collagen occurs, while the mucoid cov-

ering is confined to the surface. Outpouring of fluid into the lumen of the lower bronchioles or bronchi and osmotic intake in the upper bronchi and trachea, as a result of the temperature gradient, would be resisted; but in the ill-advised process the production of mucus is so greatly increased by proliferation of goblet cells that an excessive quantity is poured out. In addition, the viscosity of the mucus is highly increased. Anchoring of the mucous blanket to the contents of the goblet cells, together with reduction in the number and efficiency of ciliated cells, leads to stagnation of viscid secretion, with eventual blockage of the bronchial lumen, causing impaired pulmonary ventilation. Not only does the mucus fill many bronchi and bronchioles, but it even extends into alveoli; in places the extruded mass drags off the epithelium with still further loss of cilia (Fig. 4). There may be regeneration, with metaplasia to squamous epithelium.

The beneficial effect of corticosteroids appears to depend on two factors; they are reduced antibody production and decreased permeability.

Experimentally, injection of large doses of horse serum into rabbits leads to fibrinoid degeneration of small vessels, producing polyarteritis, a collagen disorder.[7] ACTH and cortisone have an effect on antibody production in immunized rabbits, reducing its level in accordance with the amount given.[1c,1d]

The second factor concerns permeability of cell walls and increase of tissue fluid. Histamine is known to cause vasodilatation, with swelling of endothelial cells, and weakening of intercellular cement; cortisone influences the terminal vascular bed and reverses the reactive hyperemia which follows local trauma, as by antigen antibody reactions, with reduction of permeability.[1e]

According to report, prednisone should be superior to cortisone.[1b] If the reaction of the tissue fluids and permeability of cell walls are reduced, with diminished reactive swelling of collagen, then abnormal reactive production of mucus is no longer required and relief to the asthmatic patient may be expected.

149 HARLEY ST.

I am grateful to Dr. Cardell for providing much information and several photomicrographs, to Professor Causey for information as to the terminal air sacs and alveoli and for the electron photomicrograph.

Professor Dohlman has kindly made various personal constructive observations on the subject.

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I am indebted to Dr. Cardell for permission to use illustrations 1, 3 and 4, and to Professor Causey for illustration 2.

LIII

OBSERVATIONS ON COLLAGEN DISORDERS OF THE UPPER RESPIRATORY TRACT

AUBREY G. RAWLINS, M.D.

SAN FRANCISCO, CALIF.

In attempting to discuss the so-called collagen diseases of the upper respiratory tract (or anywhere else in the body for that matter), the first thing that comes to my mind is the matter of terminology. Are these disorders primarily collagen diseases? I think not. Why then are they called collagen diseases? Probably the main reason is that, in the past, collagen was the one structure that stained beautifully and showed up spectacularly in stained specimens. The cellular elements were not exciting and the ground substance appeared only as blank spaces and were even called intercellular or tissue spaces. These so-called spaces are not spaces at all and they are not even filled with so-called tissue fluid. They are normally filled with a firm amorphous substance with a gel-like consistency which binds water, but in which there is no free fluid. Modern staining methods, such as metachromatic staining, gives substance and color to this ground substance while chemical and physiologic studies have given it function.

Collagen fibers make up about one-third of the mass of the body and serve mainly to hold the structures together. The word collagen means glue, and was derived from the fact that, when boiled, it turns to gelatin. It is an albuminoid protein consisting exclusively of amino acids. Practically all intercellular proteins of the body are being actively and constantly broken down and resynthesized. However, by the use of labeled substances, it has been found that there is very little turnover in collagen protein. In the absence of ascorbic acid, *no* new collagen will be formed.

The mucopolysaccharide ground substance, consisting mainly in hyaluronic acid, also helps hold the body together and adds plasticity to its structures. However, it has other important functions and one that I choose to stress is that as a circulatory apparatus. No blood

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Read as a discussion of a paper by Professor Michele Arslan before the Sixth International Congress of Otolaryngology, Washington, D. C., May 1957.

vessel supplies any body cell directly. All metabolites, bacteria, viruses, et cetera, must pass through the ground substance before reaching their destination. The consistency of this amorphous substance varies from a firm gel to a pathologic edematous sol. Hence, its circulatory function and barrier effect varies with its consistency or plasticity, and this plasticity is regulated, to a great extent, by the hormonal system.

The cellular elements of the connective tissue, consisting mainly in fibroblasts and mast cells, also have tremendously important functions. According to Asboe-Hansen, the mast cells contribute in the production of the ground substance. They also store histamine, heparin, seratonin and other substances, which are liberated in the inflammatory chain reaction. Some of these substances are inflammatory, and some detoxifying and anti-inflammatory. The fibroblasts are important in the production of collagen fibers. The work done by the University of Utah group has shown that in inflammation the mast cell granules pick up the released histamine and transport it back into the fibroblasts.

An increase in the ground substance and depolymerization or liquification of the same is characteristic of connective tissue disease. In so-called collagen disease, or any connective tissue disease, this simply means edema and this is the first pathologic finding in these disorders. Following this, fibroplasia may develop and fibronoid degeneration set in. If the condition advances, precipitates may form in the connective tissue, producing amyloid or colloid degeneration. Further progress results in an increase in collagen fibers and decrease in ground substance and cellular elements. This is the final stage of connective tissue disorders and we know it by the term fibrosis. The geriatrist would call it aging. This process does not necessarily go on this far, but in many conditions may not progress further than edema. Nasal polyps are an example of this. However, the complete process is one of cell damage, edema and progressing to sclerosis. Therefore, in so-called collagen diseases, all elements of connective tissue may be involved and collagen is probably not even primarily so. Hence, it would appear that collagen disease is not a good term and that connective tissue disease should be substituted.

Doctor Arslan has had a great experience with the unusual connective tissue disturbances in the upper respiratory tract and has presented his work in an interesting and instructive manner. I have little to add to this. However, I would like to stress the importance

of the connective tissue in the common disturbances of the upper respiratory tract. Where is the pathology in hay fever, perennial nasal allergy, vasomotor rhinitis, hypometabolic stuffy noses, or even in accidental or surgical trauma? It is mainly in the ground substance of the connective tissue resulting in edema with an increase and liquification of this amorphous substance. Dougherty has stressed the fact that inflammation, of any kind, occurs primarily in the connective tissue. Therefore, it becomes necessary to broaden our concept and consider the fact that nearly all the diseases of the upper respiratory tract involve the connective tissue. This being the case, it is essential that we be familiar with the endocrine system since the hormones function in maintaining the integrity of the mesenchymal tissues. For example, thyrotopic hormone, besides stimulating the thyroid gland to secrete its hormone, also acts directly on the connective tissue and increases the amount of ground substance and the number of mast cells. The mineralocorticoids tend to stimulate the production of the connective tissue disease while the glucocorticoids depress them. Therefore, it is likely, even though present tests are not sensitive enough to demonstrate it, that some connective tissue disorders of the upper respiratory tract are associated with hormonal derangements.

There is much to learn and much unknown about connective tissue diseases. Before the next meeting of this Congress, it is likely that great strides will be made on this subject. Newer and different concepts may come forth or more proof of our present concepts may develop. Regardless of how much further progress is made and what will be the final outcome, none of it would have been possible had it not been for the unsurpassed and fundamental work of Dr. Hans Selye.

SUMMARY

In the time allotted, I have only tried to emphasize three points:

1. Since all elements of connective tissue are involved in so-called collagen diseases, and since collagen is probably not primarily involved, it would seem that connective tissue disease is a better term than collagen disease for the disturbance under consideration.

2. The connective tissue is primarily or secondarily involved in practically all disorders of the upper respiratory tract. Hence, it would appear reasonable to broaden our concept when thinking of pathology in this area.

3. Since the hormones aid greatly in maintaining the integrity of the connective tissue, it becomes necessary for the ear, nose and throat specialist to be familiar with endocrinology.

384 Post St.

LIV

PRINCIPLES OF HEARING CONSERVATION IN SURGERY FOR CHRONIC EAR DISEASE

ARTHUR L. JUERS, M.D.

LOUISVILLE, KY.

Conservation of serviceable hearing should be a simultaneous objective with eliminating chronic ear disease. The word conservation is used here to imply improvement of preoperative hearing loss as well as preservation of useful preoperative hearing. Bondy was one of the pioneers in this phase of surgical otology. The greatest progress in this field has been made since Lempert introduced the endaural approach to the temporal bone and the use of magnification in dealing with middle ear and attic pathology. While this type of surgery can be accomplished by the postauricular route, the author prefers the endaural approach when the pathology involves primarily the attic-antral area. In the event that pathology extends into a pneumatized tip which cannot be adequately reached endaurally, a supplemental low postauricular incision may be used.

PHYSIOLOGICAL REQUIREMENTS FOR SOUND CONDUCTION BY AIR

In some instances serviceable hearing can be maintained by preserving conduction structures not involved in pathology. In others some reconstruction will be necessary. Adequate bone conduction studies must be performed before surgery to evaluate cochlear function. The following factors must exist at the completion of surgery if the optimum level of hearing is to be attained:

1. *An Inflatable Air Space over the Round Window Membrane.* The preservation or construction of even a narrow slitlike passage from the eustachian tube to the round window niche will provide this functional requirement. Of course, the eustachian tube must function sufficiently to establish equalization of middle ear and atmospheric air pressure on swallowing. Otherwise, the middle ear space will either fill with fluid or be obliterated by adhesion of the tympanic membrane

From the Department of Otolaryngology, University of Louisville Medical School. Presented before the Sixth International Congress of Otolaryngology, Washington, D.C., May, 1957.

to the promontory. The result of such obliteration would be conduction deafness. Any granulation tissue or scar tissue in the round window niche should be removed.

2. *An Intact Functioning Ossicular Chain or Contact of the Pars Tensa with the Stapes.* Obviously the most favorable situation is that in which a well functioning ossicular chain can be preserved at the time of surgery. Unfortunately, in the majority of cases, the continuity of the ossicular chain has been broken by disease, or a portion of it needs to be removed at the time of surgery in order to eliminate pathology. Approximation of the pars tensa against the capitulum of the stapes will then assure a serviceable hearing level after surgery if the stapes has normal mobility and cochlear function is good. The author has previously described this technique as myringostapediopexy.[2] Zöllner and Miodonski[3,5] used the term columella-effect for a similar procedure. Occasionally the incudomalleolar joint may be anklyosed. The preoperative hearing threshold is then usually around 50 decibels. Removal of the incus and malleus head together with a myringostapediopexy will improve the hearing to a serviceable level. It has been shown experimentally that removal of the incus without myringostapediopexy will result in only a 30 decibel hearing loss if the pars tensa is intact and the stapes freely movable. Clinically a 20 decibel level is assured if myringostapediopexy is carried out after removal of the incus if cochlear function is normal. In general, the air conduction curve here is 20 decibels below the bone conduction curve on the audiometric chart.

3. *Unimpeded Stapes Mobility.* This requirement is so obvious as to need no further comment.

INDICATIONS FOR AND OBJECTIVES OF SURGERY

The cases of chronic ear disease most amenable to hearing conservation type of surgery are those in which the pathology is primarily in the attic-antral area. The perforation is marginal in these cases and the basic pathology is usually cholesteatoma formation. Infrequently is there a suppurative process only, without cholesteatoma. The genesis of attic cholesteatoma will not be detailed here. In the author's experience, the attic retraction mechanism or epithelial migration seem to account satisfactorily for the genesis.

Surgery is indicated when one or more of the following apply:

1. Suppuration does not subside promptly under conservative treatment or tends to recur.

2. Cholesteatoma erosion of contiguous structures occurs, i.e., labyrinthine fistula, facial paresis or dural irritation (headache).

3. There is a small bottle-neck marginal perforation which tends to retain cholesteatoma.

4. X-ray evidence of cholesteatoma.

Undue delay of surgery will, in some instances, result in extension of pathology into the tympanic cavity. This increases considerably the difficulty of conserving useful hearing.

The objective of surgery as to pathology should be directed toward eliminating pathology in the attic-antral-mastoid area and exteriorizing this area into the auditory meatus so that the entire cavity can be visualized postoperatively through the external meatus. It is, in general, best to remove all cholesteatoma matrix. In carefully selected cases, it may be permissible or advantageous to preserve that portion of the matrix which extends from the pars tensa to the prominence of the lateral semicircular canal, thereby sealing off the tympanic cavity. However, the surgeon must be certain that there is no extension of pathology into the tympanic cavity or beneath the ossicular chain.

The objective of surgery as to conservation of hearing must fulfill the previously listed "physiological requirements for sound conduction by air." One of the following situations will apply as to the status of the ossicular chain as found at surgery:

1. *Ossicular Chain Intact.* If the preoperative tests indicate good ossicular function and removal of pathology can be accomplished without disturbing the chain's functional integrity, good postoperative hearing can be anticipated. The tympanic cavity must be sealed off from the attic on completion of surgery. Either a modified meatal skin flap or a free graft may be used. In some instances the medial cholesteatoma matrix may be left in situ for this purpose.

2. *Ossicles Destroyed by Disease.* I find that in most of my cases the functional continuity of the ossicular chain has been disrupted by disease. In some such cases there is serviceable preoperative hearing because the pathological changes have incidentally approximated the pars tensa against the stapes. Such cases will frequently have only a 20 decibel loss if there is no limitation of stapes mobility. This situation should not be disturbed at the time of surgery unless there appears

to be pathology under the tympanic membrane. If there is no contact between the pars tensa and the stapes, this should be accomplished after all pathology has been removed.

3. *Ossicular Chain Fixed-Removed at Operation.* If the ossicular chain is intact, but the preoperative hearing level has indicated fixation, the incus and malleus head should be removed at surgery and a myringostapediopexy carried out. If the stapes is mobile and the middle ear is free of pathology, a 20 decibel hearing level can be anticipated. If the stapes appears to be fixed, an attempt should be made to mobilize it.

4. *Ossicular Chain Intact and Functioning But Removal Necessary to Eliminate Pathology.* In the past there has at times been a tendency by some surgeons to compromise with complete removal of pathology in such cases for fear of disturbing a well functioning chain with resultant loss of hearing. Conversely there has been a tendency by others to do a complete radical mastoidectomy under these circumstances because of the erroneous concept that a 50 decibel hearing loss would result anyway from removal of the incus. If adequate removal of pathology necessitates sacrificing a well-functioning incus, carrying out myringostapediopexy technique virtually assures a 20 decibel hearing level.

When the middle ear is involved by considerable pathology (cholesteatoma or granulation tissue), the problem of restoring useful hearing is much more difficult. All cholesteatoma matrix and as much granulation tissue as possible should be removed. If there is any of the lower portion of the pars tensa remaining, it should be mobilized and its superior margin approximated against the promontory in order to create a small tympanic cavity to serve as the inflatable air space over the round window. If no pars tensa remains, a full thickness skin graft can be used to create a tympanic cavity. Serviceable hearing can be obtained if the round window niche has been cleaned out and the stapes is mobile. Creating a tympanic cavity by this technique constitutes a tympanoplasty as evolved by Wullstein[4] and Zöllner.[5] The technical details of this procedure will not be elaborated here since this discussion deals only with general principles. The author has not used the acoustic probe for testing during surgery.

CENTRAL PERFORATION

A large percentage of dry central perforations can be closed by office treatment. If there is no impedance to ossicular chain move-

ment, closure of a perforation will be accompanied by a significant improvement in hearing. Skin graft closure technique can be applied to those perforations which fail to respond to simple office treatment.

Mastoid surgery is infrequently indicated in ears with central perforations. Only if there is granulation tissue which will not respond to conservative treatment of if there is reason to suspect cholesteatoma should surgery be considered. The previously discussed principles of hearing conservation should guide the surgical technique.

FENESTRATION

If, after adequate surgery to restore useful hearing, there is still a complete or nearly complete conduction deafness, fenestration can be considered if all evidence of infection has been absent for several months. There should, of course, be an adequate tympanic cavity, a well functioning round window and good cochlear function. A good caloric response in the lateral semicircular canal should be present. Bony narrowing of the lumen of the lateral canal has been reported in cases of chronic otitis. Finally, the patient's need for improved hearing in the involved ear should be considered. If the other ear is normal, the final level to be anticipated in the deafened ear may add relatively little to the over-all hearing capacity. The need and expected benefit must be individualized in each case.

SUMMARY

1. Conservation of hearing has become an integral part of technique in modern temporal bone surgery for chronic otitis media and mastoiditis.

2. Preservation or reconstruction of some form of useful conduction mechanism is possible in most operations involving the middle ear and attic.

3. The basic requirements for effective air conduction after surgery include 1) an inflatable air space over the round window membrane, 2) contact of the tympanic membrane with the stapes if the ossicular chain is interrupted, and 3) an unimpeded stapes.

4. Accurate preoperative assessment of cochlear function is important in establishing the hearing prognosis. The final air conduction threshold will be the bone conduction level minus the residual conduction deficit.

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LV

CONTINUING CLINICAL STUDY OF LOCAL TREATMENT OF ALLERGIC RHINITIS

USE OF A NASAL SPRAY CONTAINING PREDNISOLONE ACETATE AND CHLORPROPHENPYRIDAMINE GLUCONATE

WILLIAM H. EVANS, M.D.

YOUNGSTOWN, OHIO

In the practice of medicine, as in everything else, one thing leads to another. So the present report on the results of symptomatic control of allergic rhinitis with a nasal spray containing prednisolone acetate and chlorprophenpyridamine maleate (Chlor-Trimeton) almost inevitably follows our previous studies[1-3] on topical administration of cortisone and Chlor-Trimeton, alone and in combination.

Since our earlier papers, considerable clinical and experimental evidence has accrued to furnish a firmer rationale for the topical use of corticosteroids in treatment of allergic inflammations in the nose. This rationale, briefly, is as follows: 1) medication, including the corticosteroids, is effectively and rapidly absorbed through the nasal mucous membranes; 2) corticosteroids so absorbed have a definite anti-inflammatory or "antiphlogistic" effect; 3) adrenocortical steroid hormones given systemically rapidly escape from the circulation and are deposited for a time in extravascular connective tissue; 4) studies by Dougherty and his associates[4-8] indicate that the antiphlogistic effect of corticosteroids is exerted principally by enhancing the resistance of surviving, uninjured cells (particularly fibroblasts in connective tissue) to the cytotoxic action of inflaming agents; 5) eventually corticoids are recovered unchanged in urine and feces; 6) this suggests that their therapeutic effect is brought about by contact with the tissues; 7) this finally suggests that topical administration at the site of inflammation should be as effective, if not more so, than systemic administration.

Read at the Sixth International Congress of Otolaryngology, Washington, D. C., May, 1957.

That medications of various types are absorbed through the nasal mucous membrane has been amply demonstrated. Vasoconstrictors, such as ephedrine, phenylephrine and related compounds, alone or combined with other agents, obviously must be absorbed to produce the temporary shrinking of swollen nasal mucous membranes for which they are so widely used. The anti-inflammatory effect of corticoid solutions applied topically was described in my previous papers and has been reported on by many authors. In a discussion of recent trends in nasal medication, Fabricant[9] commented that the intranasal route also has considerable merit in administration of various therapeutic agents, in that it provides rapid absorption. He cited a study comparing the effects of intranasal, oral and subcutaneous administration of hyoscine. Judged by the relative decrease in production of saliva, hyoscine was more rapidly, completely and uniformly absorbed after intranasal than after oral administration; rate and degree of absorption more nearly resembled that of subcutaneous administration. Intranasal absorption of atropine has also been demonstrated. Use of crystalline vitamin B_{12} in isotonic sodium chloride solution administered by nasal instillation to patients with pernicious anemia in relapse has produced satisfactory hematologic and clinical response, with significant excretion of vitamin B_{12} in the urine.

The effectiveness of absorption through the mucous membranes has been underlined in a report by Adriani and Campbell[10] on fatalities followng topical application of local anesthetics (particularly tetracaine) to mucous membranes. In experimental studies on dogs, they compared the rate of absorption of tetracaine from mucous surfaces of the pharynx, trachea and bronchi with those obtained after rapid intravenous injection, subcutaneous infiltration and slow intravenous infusion of tetracaine. A quantity of drug that results in no detectable blood level when infiltrated subcutaneously gives levels when applied topically to these mucous membranes that are equal to one-third to one-half of those after intravenous injection. These authors concluded that the untoward responses following topical anesthesia in clinical cases are due to rapid passage of the drug from the site of application into the systemic circulation. They state: "The absorption from mucous membrane is far more rapid than clinicians have realized and simulates intravenous administration."

The mechanism of the anti-inflammatory effect of the corticoids has been extensively studied, but is still not completely elucidated. Dougherty and his associates[8] note that adrenocortical steroid hormones rapidly escape from the circulation after administration and

that for a period of time there is deposition of the hormone in extravascular compartments of connective tissue, followed by eventual elimination in the urine and feces. It has also been shown that hydrocortisone exerts its anti-inflammatory influence locally, i.e., at the site of inflammation. This is accomplished in a dose-response fashion in that the amount of hydrocortisone required to inhibit inflammatory response is proportional to the inflaming stimulus. According to Dougherty and his co-workers, adrenocortical hormones do not inhibit the stimulus that initiates the chain reaction of inflammation. Rather, these hormones exert their antiphlogistic effect by interrupting the chain reaction of cellular destruction that is triggered by the initiating stimulus. Hydrocortisone does not completely prevent the release of products of cell injury; the evidence suggests that the antiphlogistic adrenocortical hormones exert their effect by enhancing the resistance of surviving, uninjured cells to the cytotoxic action of inflaming agent.

Dougherty et al. further suggest that all events of acute inflammation can be explained by cellular injury resulting from a lack of stabilization of the cell membrane. Attention has been focused on the fibroblast because, numerically, it is the major cell of connective tissue, and it also performs most of the functions attributed to the supporting framework of the body. If it is considered that the breakdown of one cell following injurious stimuli brings about the destruction of other cells, thus establishing a chain reaction, it must be assumed that the fibroblast is probably the central cell in this process.

"The fact that the anti-inflammatory steroid hormones exert their effects locally, focuses attention on the effect of these hormones on local connective tissue elements," according to Dougherty and Higginbotham.[4] "It has been found that following hydrocortisone administration to noninflamed loose connective tissue, the fibroblasts pull in their processes and tend to round up and resemble epithelial cells. Their cytoplasm acquires a deep basophilia, and their total appearance is very much different from that of the normal fibroblasts." Other experiments by these investigators, utilizing cytochemical and radiographic methods, show that fibroblasts concentrate the hydrocortisone within their cytoplasm. Thus it appears that hydrocortisone and other anti-inflammatory hormones may be concentrated within or at the surface of the fibroblasts, and that this concentration is followed by a change in the structure and metabolism of the affected cell which, in turn, is correlated with a greater resistance to the process of destruction in the inflamed area.[6]

CORTICOSTEROID ANALOGUES

Since the analogues, prednisone and prednisolone, are now being widely tested clinically as substitutes for cortisone and hydrocortisone, respectively, it would be expected that preparations for topical use would become available. These newer compounds have several advantages over cortisone and hydrocortisone.[11-14] They are more potent, and hence more effective, and often relieve patients whose symptoms are inadequately controlled by the older corticosteroids, as well as those who have become refractory. Side effects are greatly reduced. Because retention of sodium and water are minimal, prednisone and prednisolone can be used in conditions where older steroids were contraindicated or presented great risk. Enhanced potency and reduced incidence of side effects permit long-term, continuous administration with greater safety in many chronic diseases.

While these advantages are not so significant with regard to topical administration in allergic rhinitis as they are when the corticoids are taken systemically, it is nevertheless desirable, at least in theory, to avail ourselves of the greater safety that they provide. In our experience, there has never been any evidence of ill effect from the topical use of cortisone in the nose, even when it was used at intervals over several years, and to my knowledge no such complication has been reported. Nevertheless, cortisone and hydrocortisone are known to be potentially dangerous, and require careful management when given systemically; hence this should always be kept in mind, even when they are being used locally. Now that less hazardous agents with the same desirable therapeutic effects are available, these should be evaluated for every clinical situation, including their topical administration.

The topical use of prednisone and prednisolone has been assayed in several series of ophthalmic inflammations. In an interesting experimental study reported by Leopold, Kroman and Green,[15] it was found that penetration studies following systemic administration of the steroids suggest a relationship between rate and degree of penetration and relative therapeutic effectiveness; this is not borne out by local penetration studies. The older steroids, cortisone and hydrocortisone, were less effective in inhibiting inflammation than prednisone and prednisolone, but the former penetrated the tissues more easily following local application. Hence the clinical effectiveness apparently is dependent upon some other inherent physiologic property,

rather than on individual penetrative ability. Hogan and co-workers[16] found that prednisone and prednisolone solutions, 0.5 per cent, were as effective as hydrocortisone acetate suspension, 2.5 per cent, in controlling surface lesions of the conjunctiva and cornea when applied topically. Weaker solutions were not as effective. Experimental studies on rabbits suggested that topical therapy with prednisone and prednisolone might be expected to activate latent herpes febrilis infections in the same manner as hydrocortisone has done. No instance of such activation, however, was detected in over 200 treated cases. In another study by Gordon,[17] preliminary evaluation indicated that prednisone and prednisolone are clinically superior to cortisone and hydrocortisone when used topically in the eye. In a clinical and experimental investigation of the new corticoids, King and Weimer[18] concluded that their antiphlogistic activity appears superior, in most instances, to that of cortisone and hydrocortisone. Several patients who responded poorly, or not at all, to other steroids, showed dramatic improvement with prednisone and prednisolone. The effectiveness of prednisone and prednisolone in local eye therapy was confirmed by these authors in later studies.[19] Abrahamson and Abrahamson[20] used a combination of prednisolone, sodium sulfacetamide and neomycin in over 350 cases of ocular inflammation of various types, either as drops or ointment, with few untoward effects. Comparison of cortisone and prednisolone products showed little difference in results, both being equally effective, although prednisilone was somewhat more rapid.

In a series of 128 dermatologic cases in which a therapeutic assay of topically applied prednisolone was made and compared with that of hydrocortisone, results reported by Zimmermann[21] indicated that prednisolone alcohol, when used in only one-half the concentration of the hydrocortisone free alcohol, is as effective as, or slightly more effective than hydrocortisone free alcohol. Cases of contact dermatitis, atopic dermatitis and pruritus ani were treated. Thus it appears that, in topical application, prednisolone is approximately twice as effective, milligram for milligram, as hydrocortisone.

PRESENT CLINICAL STUDY

The preparation that has been used in this series of clinical cases is a suspension containing 2 milligrams (0.2 per cent) per cubic centimeter of prednisolone acetate and 3 mg (0.3 per cent) of chlorprophenpyridamine gluconate (Chlor-Trimeton) in a non-irritating isotonic vehicle. This is dispensed in a plastic atomizer bottle, which

emits a very fine spray, and may be used every three or four hours to relieve nasal blockage, sneezing and mucosal irritation. Two variants of this combination have also been tried, the one containing these same ingredients with phenylephrine, and the other with phenylephrine and neomycin.

In our previous reports concerning local treatment with cortisone and Chlor-Trimeton suspensions, we recommended use of nasal packs or drops (to be instilled while the patient was lying down) because these appeared to yield better distribution of the solution over the nasal mucosa than the usual nasal atomizer.[2,3] With the newer preparations available in the plastic spray bottle, we now believe that this method of administration is equally satisfactory, since the spray emitted is fine enough to reach all parts of the nasal lining, and it has the practical advantage of being much easier for the patient to use. The small bottle can be carried in the pocket or purse and used conveniently whenever symptoms require, whereas circumstances do not always allow one to assume a horizontal position in order to instil drops into the nose.

The prednisolone-chlorprophenpyridamine nasal spray is used in the majority of cases of allergic rhinitis as adjuvant therapy. Many of the patients have been followed for many years and have had various types of treatment, including systemic and topical antihistaminics of various types, specific desensitization, antibiotics, etc. Many had previously received treatment with the earlier preparation of cortisone and Chlor-Trimeton, as nose drops.

During the past fifteen months, in almost all cases of nasal allergy requiring continued symptomatic treatment, the cortisone-Chlor-Trimeton solution has been replaced by the prednisolone-Chlor-Trimeton suspension. Some new patients have received the new nasal spray as initial therapy.

Eighty patients have used the prednisolone-Chlor-Trimeton nasal spray, 37 the prednisolone preparation with phenylephrine added, and 21 the product with added phenylephrine and neomycin. Eleven in the second group and 2 in the last group also were among the 80 who received the basic preparation containing only prednisolone and Chlor-Trimeton. The total number of patients, with sufficient follow-up for evaluation, was 125.

The results of topical application of the prednisolone preparations were satisfactory in the great majority of instances, both subjectively

and objectively. Some individuals, however, who had used some of the earlier preparations, reported that they were not able to distinguish much difference in the amount of relief obtained with the newer suspension. Most patients preferred the use of the spray bottle to the instilling of drops. Nevertheless, in small children, our impression is that the medication can be more effectively applied with a dropper. Generally, those who had previously used the cortisone preparation with satisfactory results continued to be effectively relieved when the preparation was changed. There was much less complaint of burning or irritation with use of the newer nasal spray. On the basis of clinical observations, addition of phenylephrine and neomycin apparently did not enhance the therapeutic effectiveness of the preparation significantly. Repeated nasal smears and bacteriologic studies were not made in the majority of instances in this series. Solutions containing phenylephrine appeared to be a little more effective in relieving nasal blockage, but we have seen no evidence that addition of the antibiotic provides any extra advantage in nasal allergy.

Among 27 patients who received the prednisolone-Chlor-Trimeton suspension alone, relief was satisfactory in 23 and fair in three. Prednisolone suspensions containing phenylephrine and neomycin produced good results in 22 and fair results in six patients who received no other treatment. In 25 cases, symptoms were well controlled by use of the basic topical suspension along with some antihistaminic by mouth. An additional 24 patients had fair relief with this combination. In 9 cases, good or excellent relief was obtained by desensitization, oral use of an antihistaminic and the prednisolone spray. One patient failed to obtain relief by means of the prednisolone suspension and an oral antihistaminic, but improved markedly when small desensitizing doses of histamine were given. In one case, corticosteroid was given orally, along with an antihistaminic and topical prednisolone-Chlor-Trimeton. In one case, the topical suspension, cortisone and an antihistaminic by mouth were combined with hyposensitization. Local nasal treatment was helpful in affording relief in some cases.

Thus, among 125 patients who used the prednisolone nasal suspensions, 115 obtained significant relief from them, either as the sole therapy or as a component of more comprehensive antiallergic treatment. It should be remembered that these were all private patients. Hence the prime consideration was to relieve their symptoms as rapidly and effectively as possible by whatever measures were dictated by the clinical situation.

COMMENT

The anti-inflammatory effect of cortisone and hydrocortisone and of their analogues, prednisone and prednisolone, has been amply demonstrated in our several series of cases, and by numerous other workers, whose observations have been cited in our previous papers.[1-3] Flynn[22] has recently reviewed and summarized the uses and abuses of the adrenocortical steroids in otolaryngology and their effects following both systemic and local administration. As has been true since the advent of cortisone therapy, the number of reports on topical administration in allergic diseases, particularly in allergic rhinitis, has remained small in relation to the number of contributions on the therapeutic results of systemic administration. This holds true ıor the newer analogues as well as the older corticoids. The most recent reports have concerned the use of hydrocortisone, generally speaking. The topical use of prednisolone in ophthalmic and dermatologic inflammations has already been cited.

In a study using cortisone and Chlor-Trimeton suspension in treatment of 153 patients with allergic rhinitis, Seidmon and Schaffer[23] reported good to excellent relief in 132 (86.3 per cent). Only 11 (7.2 per cent) failed to obtain any relief, and the results were better than those obtained with antihistamine alone. Silcox[24] reported a study on 174 patients suffering from allergic rhinitis, with and without polyps, and acute rhinitis. Preparations evaluated were: a 5 mg per 100 cc suspension of cortisone alcohol; a 50 mg suspension per 100 cc of hydrocortisone alcohol; 22 mg per 100 cc, 20 mg per 100 cc and 2 mg per 100 cc of hydrocortisone alcohol, a 20 mg per 100 cc solution of hydrocortisone alcohol containing two vasoconstrictors, hydroxyamphetamine hydrobromide and phenylephrine hydrochloride; a solution containing the vasoconstrictors alone, and an isotonic saline solution. Medications were given four times daily, with the plastic spray bottle. The cortisone alcohol solution proved ineffective in all conditions; all the hydrocortisone alcohol solutions caused a significant beneficial effect on allergic rhinitis, with and without polyps. Polyps were sometimes reduced dramatically, but temporarily. The solutions were of no value in acute rhinitis. The 20 mg per 100 cc solution of hydrocortisone alcohol combined with the vasoconstrictors proved the most effective medication. This was significantly beneficial, and exerted a marked anti-inflammatory action, besides providing effective subjective relief.

A similar experience with the same preparation was reported by Pennypacker[25] in 23 patients with ragweed hay fever, half of whom

had failed to respond to desensitization or antihistamine therapy. Fourteen had significant improvement, both objectively and subjectively. No predictable relationships between nasal eosinophil counts, subjective or objective response to treatment, or day-to-day counts of pollen during the ragweed season could be elicited.

Controlled studies by Burger and Shaffer[26] in topical application of various preparations of hydrocortisone in several concentrations in 200 patients with vasomotor rhinitis demonstrated a marked anti-inflammatory effect and symptomatic improvement in 76-86 per cent of patients using hydrocortisone suspensions. Hydrocortisone free alcohol solution in a concentration of 0.2 mg/ml was effective in 64 per cent. No significant systemic absorption, adverse effects, change in nasal exudate, or alteration of the histologic appearance of nasal polypi were noted after therapy.

Smith[27] found the local application of a 2.5 per cent suspension of hydrocortisone acetate in nasal jelly of value in patients with nasal allergies, especially in the milder, less reactive group. When this local therapy was combined with specific hyposensitization by Hansel's method, the effectiveness of both appeared to be increased.

We have used the hydrocortisone preparation containing the two vasoconstrictors in numerous cases, with results comparable to those reported by the foregoing authors. Long-term systematic study of this preparation was not carried out, however, because, when the prednisolone suspension appeared, it seemed feasible to concentrate attention on it.

Another study with topical hydrocortisone (as drops) was reported by Rohen[28] who used a suspension of 20 mg of hydrocortisone per cubic centimeter in cases of allergic and of infectious rhinitis. Although in cases of the latter with fever, an antibiotic was given to bring it under control. No antibiotic was added to hydrocortisone in local treatment. In treating allergic rhinitis, no antihistamine was added. Contrary to the usual experience, Rohen reported equally good results with hydrocortisone in both allergic and infectious nasal inflammations.

Topical administration of hydrocortisone snuff (powder) resulted in complete control of symptoms and excellent initial response during the first two weeks of treatment in 23 of 24 patients with severe hay fever treated by Herxheimer and McAllen.[29] Dose of the powder

was 15 mg. Of 19 patients followed, 8 discontinued the snuff within three weeks and had no relapse. The rest were satisfactorily controlled with the powder throughout the whole season. These patients had not responded to previous therapy, including antihistamines to the limit of tolerance.

Dunn[30] has reported an interesting series of cases of allergic rhinitis treated with a nasal antibiotic solution, both with and without hydrocortisone, to illustrate his point that the infectious component in allergic rhinitis should not be neglected. Anti-allergic therapy is not sufficient in many instances. Clinical improvement in the cases he treated with antibiotic solutions was accompanied by disappearance of leucocytes from the nasal smears. Although addition of hydrocortisone to the antibiotic solution did not alter the findings in the nasal smear, it apparently increased rapidity of therapeutic activity and the duration of symptomatic relief.

A hydrocortisone-antibiotic combination containing hydrocortisone alcohol, hydroxyamphetamine hydrobromide, phenylephrine hydrochloride, gramicidin, neomycin sulfate and polymixin B, was used by A. H. Persky[31] in a study of 109 patients with acute respiratory infections or infections superimposed on some underlying pathologic condition. Objective results were considered good or excellent in 91, fair in 10 and poor in 8. Subjective results were good or excellent in 82, fair in 18 and poor in 9. For most patients it was well tolerated, effective treatment, providing immediate and long-lasting relief of five to six hours from nasal congestion. It also decreased bacterial activity considerably and ameliorated nasal inflammation.

A controlled study of prednisolone used topically was reported recently by Anderson and Ogden.[32] Each patient received a placebo, a 0.1 per cent and a 0.5 per cent solution of prednisolone, each for one week. Between each treatment period, a rest interval of one week was inserted to avoid carry-over effect. Patients applied the nasal spray (one squeeze of the bottle into each nostril) every half hour while awake for the first 48 hours; afterwards dose was reduced to one spray in each nostril four times daily. None who received the placebo showed any clear subjective or objective improvement. All patients reported improvement with the prednisolone solutions. Twenty-four had more improvement with the 0.5 per cent solution than with the 0.1 per cent solution; most of these had only moderate metaplastic change in the nasal mucosa. Six who reported greater improvement with the stronger solution had more advanced nasal allergy or

had had previous nasal operations which interfered with normal nasal mucosal function. In five patients with polypoid degeneration, there was no decrease in size of the polyps. These authors stressed the importance of careful selection of cases and initial saturation of the nasal tissues to obtain good results with this or other topical steroid therapy in the nose.

Our own cases and the reports just cited furnish convincing proof of the efficacy of the corticosteroids and their analogues when applied topically to inflamed nasal mucosa in allergic conditions. Since prednisolone, generally speaking, appears to be safer and more effective than hydrocortisone (or as effective), it would appear, at present, to be the preparation of choice for this purpose. In practically all cases, the results obtained with prednisolone-Chlor-Trimeton suspension parallel those observed with the older cortisone and hydrocortisone preparations, athough an occasional patient claims to experience greater relief with one or another preparation. In the peak of the various pollen seasons, only the mildest cases of nasal allergy, as a rule, can be completely controlled by means of topical treatment with the prednisolone-Chlor-Trimeton suspension and similar corticoid preparations. Nevertheless, the use of these suspensions affords considerable additional relief when used as an adjunct in the treatment of nasal allergies, along with antihistaminics by mouth, vasoconstrictors and desensitization procedures, alone or in various combinations.

510 Dollar Bank Bldg.

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LVI

OPTIMAL DOSAGE THERAPY IN ALLERGY AND IMMUNITY

FRENCH K. HANSEL, M.D.
ST. LOUIS, MO.

Optimal dosage therapy is based upon the principle of the parenteral introduction of various allergenic, antigenic and other agents in the smallest amount or dilution which will produce a satisfactory physiologic, immunologic or pharmacologic response. Such effective doses are increased or decreased usually within a range of not greater than a multiple of ten. The duration of effectiveness varies from hours to a few days, sometimes longer, and the intervals between the introduction of the agent concerned cannot be increased to produce a longer period of response without causing a reaction or upsetting the physiologic balance. As a rule longer intervals of effectiveness occur gradually after prolonged therapy, varying, of course, with the particular agents introduced.

Although the optimal dosage principle is not new, the method has been followed only by a comparatively small number of observers. On the other hand the method of so-called "desensitization" has been more popular and has been employed almost exclusively by the allergist and the immunologist. It is based upon the principle of beginning treatment with a small dose, usually somewhat greater, however, than the optimal amount and gradually increasing it at intervals of five to seven days until a maximum of tolerance is reached as manifested not infrequently by the appearance of a local or a constitutional reaction.

In the following discussion evidence will be presented to show that the protective effect of optimal dosages is not based upon the same principle as protection from "tolerance" produced by the maximal dosage.

MAXIMAL DOSAGE OR DESENSITIZATION

Early experiments on guinea pigs and rabbits demonstrated that the state of antianaphylaxis or refractoriness could be produced fol-

Presented at the Sixth International Congress of Otolaryngology, Washington, D. C., May, 1957.

lowing the constitutional reaction induced by a large dose of antigen. This method of treatment of allergic diseases in man is now generally employed. A maximal dosage of antigen is established always avoiding, if possible, severe constitutional reactions. More recently, a booster method of treatment for ragweed hayfever has been introduced by which only about six injections are given. The dosage is rapidly increased, in spite of mild general reactions and after a rest period, a booster dosage is given to produce a state of refractoriness. Another rapid method by which only six or eight injections are given consists in the use of antihistamines before, during and after the injection.

With the introduction of the use of horse antisera for the treatment of diphtheria, tetanus and pneumonia, large doses of 50 to 100 cc were employed. Serum sickness reactions occurred in about 85 per cent of the patients so treated. Later the incidence was reduced to an insignificant minimum by refinement of the sera and the reduction of the amount injected to not more than a few milliliters. Occasionally, however, sensitivity to antisera occurs even with this small dosage. Attempts to desensitize patients hypersensitive to sera by use of rapid methods has not been satisfactory or free from the risk of severe constitutional reactions; even when protection or tolerance is established it lasts for only a short period of time.

Urbach's[1] modification of this method designated as "Skeptophylactic de-allergization" was employed according to the following plan. In a case of dermatitis caused by nickel, a positive patch reaction was noted to a 1-1,000,000 dilution. Treatment was instituted by beginning with an initial dose of 0.10 cc of the 1-100,000,000 (No. 8) dilution. Two injections were given daily, the first dose in the morning and the second 12 hours later. Both dosages were increased daily, the afternoon one being ten times stronger than the one in the morning. In this manner a top dosage of 0.10 cc of the 1-100 dilution was quickly reached but marked local and focal reactions developed. Treatment was readjusted so that the morning dose was 0.10 cc of the 1-700 and the afternoon 0.10 cc of the 1-70. After this course of treatment a patch test with an eleven per cent dilution of nickel produced only a slight reaction. The patient was able to continue contact with its products provided the hands were not immersed in the solutions.

THE MECHANISM OF DESENSITIZATION

Bronfenbrenner[2] states that typical anaphylaxis occurs only under artificial circumstances such as following the injection of relatively

large doses of antigen into the circulation of animals sensitized seven to ten days previously by the injection of the same antigen.

If instead these animals receive a relatively small test dose of antigen, larger doses, if injected slowly, or highly diluted or if the injection is given three to four days following the initial exposure, acute anaphylaxis does not occur. Subacute anaphylaxis, however, may result after recovery from which the animal may tolerate a dose several times greater than the lethal one.

Besredka[3] designated this refractory state, which lasts only hours or days, as one of "antianaphylaxis." It is only relatively effective and may be overcome by increasing the test dose of antigen. This temporary state of refractoriness or loss of sensitivity has been assumed to be the result of an antigen-antibody reaction. This phenomena has been referred to as "desensitization." Bronfenbrenner points out that this term is highly misleading and has obscured the true facts by suggesting that the level of antibody determines the type of reaction of the animal to the antigen.

In the so-called desensitization treatment for hay fever it is assumed that protection results from the production of an excess of circulating antibodies. Such assumption does not account for the fact that previously sensitized animals may be made immediately refractory by the single injection of large but sublethal dose of antigen before antibodies are demonstrable.

A similar state of refractoriness may be produced by the injection of increasing doses of antigen given within a few hours (horse serum desensitization in man). These procedures do not involve the immediate production of additional antibody for it does not appear until several days later and by that time the refractoriness has disappeared and the original hypersensitivity has returned.

Bronfenbrenner also states that immune animals with a high concentration of antibodies against pneumococcus polysaccharides may be killed by anaphylactic shock from the intravenous injection of a mere trace of polysaccharides. From these observations it was concluded that excess of circulating antibody does not produce the state of refractoriness or antianaphylaxis. The effectiveness of "desensitization" must, according to Bronfenbrenner, involve some other mechanism so the term is a misnomer. Desensitization is never complete but only relative and lasts but a short period of time. The refractory state is not specific, for other antigens may show diminished reactivity

at the same time. Anaphylactic agents such as pepsin and trypsin may also produce anaphylactic-like responses. The injection of trypsin produces anaphylaxis and the liberation of histamine.

According to Bronfenbrenner the true mechanism responsible for the refractory state may be explained as follows: as the serum tryptase becomes activated the products of its digestive activity have a tendency to delay or even arrest further activity of the enzyme. They exert so-called "antitryptic" activity. Some of these products have been recognized as polypeptides. Irrespective of the method by which a rise in antitrypsin is produced, either by specific or nonspecific means, animals remain refractory to anaphylaxis so long as the antitryptic titer remains elevated.

REAGINIC AND BLOCKING ANTIBODIES

Instead of "reagin," Sherman[4] recommends the simple description term, "skin sensitizing antibody." The more dilute the serum the higher the concentration of antigen required to produce a detectable reaction, with passive transfer. Bradel[5] found that the fluid of nasal polyps contains sensitizing antibodies in concentrations as much as 40 times greater than that present in the serum from the same patient.

The skin-sensitizing antibody is characterized by its thermolability. Heating to 56° C for one-half to four hours destroys its activity. This property is species specific for human serum as no change occurs from heating rabbit serum. The SS antibody is found in the alpha, beta and gamma globulins. Other antibodies are contained only in the latter fraction.

The injection of pollen antigen into nonallergic persons does not produce SS antibody. The injection of heterologous antisera and Ascaris antigen, however, will produce them in man. Antibodies capable of sensitizing human skin may be produced in rabbits and guinea pigs by the injection of pollen, horse serum, egg albumin and other antigens. The skin sensitizing activity of the guinea pig antisera is not correlated with the titer of anaphylactic antibody. Sherman also points out that there is no quantitative relationship between the precipitin content and the sensitization of human skin. Although the artificially produced SS antibodies are specific, the specificity of naturally occurring SS antibodies is rather vague. Cross-neutralization experiments with the sera of individuals with multiple sensitivities show many cross reactions to unrelated allergens. The variations

in the amount of SS antibody in hay fever treated patients as determined by the dilution test and the neutralization point, do not run parallel. Cooke and his associates[6] found that this was the result of a blocking or inhibiting type of antibody which is thermostable and competes with the SS antibody for antigen. Sherman believes that there is good evidence that the tolerance of the patient for progressively larger doses of pollen extract may be correlated with the development of blocking antibody, which protects the patient from constitutional reactions. It was finally concluded, however, that there has been no significant correlation between blocking antibody titers and clinical results.

In discussing the serologic differences between spontaneous and induced allergies, Cooke[7] points out that with the latter sensitivity (serum sickness) antibodies of the skin-sensitizing, muscle sensitizing and precipitating types are present, while in spontaneous (atopic) sensitivity only skin sensitizing antibodies are found. With induced allergy there is a rapid decrease in the antibodies concerned. In spontaneous allergy no abnormal electrophorectic pattern has been noted in the serum but with induced sensitivity Cooke found a distinct, early dysproteinemia but after 56 days all values were normal. In the latter type the major part of the skin sensitizing antibody lies in the gamma globulin fraction and the alpha$_2$ globulin plays no part as a cause of reactivity. Some reactivity, however, may be associated with beta globulin. In spontaneous allergy reactivity is associated with all the above fractions.

AGAMMAGLOBULINEMIA, ALLERGY AND IMMUNITY

Recent observations by Good[8-10] and others have disclosed some interesting phenomena of immunity associated with agammaglobulinemia. These patients are unable to produce useful quantities of circulating antibodies. There is a striking difference in response to pyogenic and viral infections. One of Good's patients, a young boy, had multiple severe bacterial pyogenic infections but he became immune to such viral infections as measles and chicken pox after a single attack and he had no more than the normal number of colds.

Good sensitized normal volunteers and some of his patients with 2,4-dinitrofluorobenzene, which sensitizes practically everyone. Normals and agammaglobulinemics reacted exactly alike. After a sensitizing dose, small test doses produced positive reactions in both. Tests with hybrid bacterial protein allergens, showed again the same response

in both groups indicating that something other than gamma globulin is involved in this mechanism. Good designates this phenomenon as "cellular allergy" in contrast to that of allergy in which reagins and globulin antibodies are in the serum.

When agammaglobulinemic patients are vaccinated the immediate response is much the same as in normals. The response to re-vaccination is quite like the "cellular sensitivity" reaction. Consequently, cellular sensitivity, vaccination response and agammaglobulinemic resistance to viral infections may involve a common mechanism.

Good also points out that agammaglobulinemic patients appear to be susceptible to collagen diseases such as rheumatoid arthritis, scleroderma, dermatomyositis and Lupus erythematosis. This refutes the belief that gamma globulin antibodies are a factor in collagen diseases and suggests that, instead, the cellular sensitivity mechanism plays the important part. Since the mechanism involves the cells the concept of enzymatic adaptation seems logical.

THE ENZYMATIC CONCEPT OF ANAPHYLAXIS AND ALLERGY

During the past few years a great deal of attention has been directed to the part played by cellular enzymes in health and in disease. Evidence has been presented to suggest or indicate that the mechanism of anaphylaxis and allergy is based upon the enzymatic rather than the antigen-antibody concept. More recently Godlowski[11] and also Sevag[12] have presented convincing evidence of the validity of the part played by cellular enzymes and hormones.

Godlowski believes that anaphylaxis and allergy are identical conditions differing mostly in the degree of reaction. The enzymatic concept concerns the alteration of intracellular and extracellular proteolysis. Hypersensitivity is a condition in which toxic enzymes appear in the involved cells as the result of allergenic or antigenic action. The sensitizing dose of the exciting agent, upon entering the cell, causes the production of toxic protease, a second "shock" dose initiates toxic proteolysis which liberates toxic breakdown products intracellularly. The normal enzymatic system is adapted to the disposition of these agents without any reaction. This occurs chiefly in the lymphatic system at the portal of entry.

In the state of hypersensitivity, Godlowski advances the following concept of the various stages of anaphylaxis. In the first stage

the reaction occurs at the cellular level and no clinical manifestations are evident. In the second stage the toxic proteolysis becomes extracellular with the production of local manifestations. In the third stage the reaction becomes generalized with the production of constitutional manifestations associated with focal signs such as generalized urticaria or acute bronchial asthma. In the fourth stage, there may be a total recovery from the "Metabolic Storm" or there may be only partial recovery with permanent injury or destruction of certain cells. A state of chronic anaphylaxis may occur or focal necrosis may appear in the shock organs. Finally the reaction may be of such severity as to cause the death of the organism.

With the use of the optimal dosage method of therapy very small amounts of allergen are introduced which apparently stimulate the protective enzymatic mechanism so that local or general manifestations are either attenuated or prevented. Since the effective doses are not increased beyond the physiologic level the various stages of so-called anaphylactic or constitutional reactions are not produced. As a consequence evident cellular or tissue damage never occurs and the patient does not become worse with continued treatment. Eventually, however, normal enzymatic adaptation may be restored, in some instances to the state at which no further symptoms of allergy are manifest.

NORMAL TOLERANCE

The enzymatic mechanism of the normal individual is capable of disposing of a great variety of substances which enter the body. Sevag, however, states that a foreign substance cannot escape the consequence of reacting with and modifying protein molecules. The body cells must either destroy these substances or suffer the consequences of one or more metabolic modifications.

The great variety of agents such as drugs and other therapeutic agents, toxic substances, chemicals, etc., which are tolerated by the human system is truly amazing. When normal tolerance is overstepped, however, evidence of cellular damage occurs with the symptoms and signs of disease. Such toxic effects must be distinguished from the development of the state of hypersensitivity or allergy. The latter may be induced by a small rather than a large amount of foreign substance. Hypersensitivity to pollen, for example, may occur from a small fraction of a milligram of active substance. In the case of therapeutic sera, or penicillin a fairly large amount of substance is usually necessary to induce a serum sickness type of reaction. In either instance, however, the development of hypersensitivity is greatly

dependent upon the predisposition of the individual. Those with a strong family history of allergy or those who already have some existing manifestations are more readily sensitized.

After the state of hypersensitivity is induced, the difference in tolerance to the sensitizing agent is one of great magnitude. A normal individual may, for example, tolerate a million or more units of penicillin in one dose. After hypersensitivity has developed, however, a general or even fatal reaction may occur to a fraction of a unit of penicillin. Bierlein[13] recently reported the case of such a patient who had a severe general reaction following the intradermal injection of three/one-millionths of a unit of penicillin. The allergenic dose is always small, sometimes minutely small, so must be appreciated as such.

Brown[14] reported the case of a patient who died of exfoliative dermatitis following the ingestion of 8 mg of phenobarbital. He estimated that this amount of drug dissolved into the total body water content, amounted to a dilution of 1:250,000,000. He also pointed out that the minimum serum concentration of penicillin necessary to inhibit penicillin sensitive organisms is in the same order of magnitude, namely, 1:50,000,000, although allergic responses are caused by higher dilutions affecting many more cells much more devastatingly. A constitutional reaction may occur from a skin test with a solution containing 0.0001 mg of active protein per cc.

THE CLINICAL APPLICATION OF THE OPTIMAL DOSAGE TECHNIQUE

In the use of the so-called desensitization method, it has long been known that the first small initial doses of allergen were followed by striking improvement of short duration. Because of the necessity of repeating such injections at frequent intervals such as once or twice daily or every 24 to 48 hours, the method has not been generally adopted as practical and economical. As subsequent doses are increased their therapeutic effect is soon lost and if increased too rapidly local or general reactions may occur. This is particularly noted in the treatment of pollinosis. These early reactions, however, are usually followed by an increased tolerance as the result apparently of the production of antianaphylaxis so further increases are not likely to be followed by reactions until a maximum dosage is reached.

Because of the occurrence of these reactions and the poor end results often noted, we[15] abandoned this method of treatment more

than twenty years ago, in favor of the optimal dosage plan. Our experiences, as well as those of others previously reported, will be presented briefly in the following discussion.

In 1922, Vaughan[16-17] treated a few ragweed sensitive patients by the coseasonal method, with the injection of 20 to 80 units at 1 to 3 day intervals. The results were strikingly good. In our geographical area, this dosage would be too large as our pollen counts are much higher than those of the Virginia area. During a subsequent season, however, his results were not good when the dose was progressively increased, so the conclusion was reached that the dose must be optimal.

In 1932 Anderson[18] reported his results on the use of the coseasonal method in which small doses were used but they were increased during the season. His idea of the small dosage was based upon the fact that only a few pollen grains will excite symptoms and in terns of pollen extract the patient breathes only a few units in 24 hours even at the height of the season.

In 1932 Crowe[19] reported his observations on the use of bacterial vaccines in the treatment of a large series of cases of rheumatoid arthritis. He employed the optimal dose principle with excellent results. Vaccine dosages as low as ten organisms per cc were effective. In some instances, reactions were induced, even with these small doses.

In the treatment of contact dermatitis among penicillin handlers, Morris-Owen[20] reported recently that by the daily injection of a small dose of penicillin, the patient could be conditioned for work without skin eruptions. The doses varied from one to five units down to 1/100 of a unit. Attempts to increase the dose above the optimal were followed by severe dermatitis and as a result of the flare-up, the optimal dose was difficult to reestablish until a prolonged rest period was allowed.

The effect of the small optimal dose may be evident in 20 to 30 minutes and lasts usually from 12 hours to as long as 72 hours, depending upon the nature of the allergenic agent and the degree of existing hypersensitivity. In the management of a case of marked hypersensitivity to insulin in a young man, Burden[21] found that about 30 to 45 minutes after the intradermal injection of 1/100 unit of insulin (which was the end point of reaction determined by serial dilution testing) the patient could tolerate the required daily therapeutic dose of 25 units without a reaction. Another small optimal dose was given

12 hours after the first one in order to carry the protection until the 25 units of insulin was consumed. This method is applicable in the use of other allergens such as sera, penicillin, etc. Serial dilution titration testing should be performed to determine the end point of reaction and the initial optimal dose.

THE THERAPEUTIC INTRODUCTION OF ALLERGENS AND ANTIGENS

In the therapeutic use of these various agents, a number of routes may be employed for introduction such as: 1) the intracutaneous or intradermal, 2) subcutaneous, 3) intramuscular, 4) intravenous, 5) intrathecal, 6) nasal, 7) sublingual, 8) oral and 9) rectal. The route employed depends upon the nature of the particular agent selected and the effect to be desired.

In the injection of such allergens as house dust, molds, pollens and miscellaneous inhalants such as dog, cat, horse and feather dander, etc., we prefer employing, as a rule, a 26 gauge, ¼ inch needle and giving the injection deep intradermally. In using this method, however, the amount injected must be small, from .02 to .10 cc. Since all dilutions are prepared in a series of ten, the amount can be adjusted to the dilution. For example, instead of injections of 0.20 cc of a given solution, 0.02 of the next (ten times stronger) solution is employed. With the injection of these various agents, we usually use in addition, daily sublingual doses of the same material to maintain a constant and frequent introduction of the allergen. The injections really serve as boosters.

For each allergenic or antigenic agent, the most effective optimal dosage must be determined. The duration of effectiveness varies with each substance. The intervals between injections may vary from 6 hours to two or three weeks. As therapy is continued, longer periods of effectiveness with such allergens as house dust and other inhalants, are usually possible. In the case of pollen, the intervals are usually short, six to 72 hours. As a rule, the more potent the allergenic agent, the greater the degree of hypersensitivity. Smaller optimal doses are usually indicated and the period of duration of effectiveness is short.

In the introduction of the initial dose for therapy, serial dilution testing, or titration, may be of value in some instances. The end point of reaction in the case of pollen, penicillin, sera, insulin and

other allergens equally as potent, represents the average initial dose. With the miscellaneous inhalants such as house dust, atmospheric molds, animal danders, etc., the end point of reaction is usually at a much stronger dilution than that employed as the initial dose, so is not of much value.

All materials used for testing and treatment are prepared in serial dilutions of ten beginning usually with a concentrate as follows: 1-10 = 10^{-1} or No. 1, 1-100 = 10^{-2} or No. 2, 1-1000 = 10^{-3} or No. 3, etc. The optimal dosage ranges for certain agents in doses of 0.02 to 0.10 cc may be employed as follows:[23-24]

1. Pollens: trees, grasses and weeds, No. 5, 6, 7 and 8. Average for adults, No. 5 and No. 6; for children, No. 7 and No. 8.

2. House dust, atmospheric molds (feed mill dust) and other miscellaneous inhalants: No. 5, 6, 7, 8, 9, 10, 11 and 12. For adults with nasal allergy, No. 5, 6, 7 and 8. For nasal allergy and asthma, No. 9 and 10. For children with nasal allergy, No. 8 and 9. For asthma, No. 10, 11 and 12. Dosages must be manipulated according to individual cases. As a rule smaller doses are employed for the more severe and for those with secondary food allergy or with active pollen symptoms.

3. Histamine: for headaches, vertigo, etc., No. 6, 7, 8 and 9. Average No. 7, stronger No. 6, weaker No. 8 and occasionally No. 9, especially for vertigo. Dosage usually every 3-4 days. Later 7 to 10 days.

VACCINES

Staphylococcus Toxoid. For acute respiratory bacterial infections, styles, furunculosis of the ear canal, boils, acne, seborrheic dermatitis, it is most effective.[22-23] This is also effective in stimulating immunity in those instances in which it is low as the result of antibiotic therapy. Average dose 1/100 unit intracutaneously every three to four days. For children average dose 1/1000 unit.

For allergic dermatitis, 1/10 to 2/10 unit every three to four days. Children, 1/100 to 1/1000 unit doses. The larger doses for allergic dermatitis and penicillin reactions apparently produce an ACTH stimulating effect. The small doses used for bacterial infections stimu-

late immunity. Some anamnestic response usually follows for other bacteria, such as streptococci, pneumococci, etc.

Trichophyton, Monilia, Epidermophyton. These pathogenic molds may be employed individually or as a mixture.[23] Dilutions of 10^{-7} or 10^{-8} are usually administered intradermally in doses of 0.02 cc to 0.10 cc every three or four days. These mold extracts are indicated in certain cases of external otitis, ringworm of the face (especially the eye brows and the scalp). Monilial extract, also known as monilin or oidiomycin, is especially effective in the oral and intestinal moniliasis secondary to antibiotic therapy. We usually combine it with Staphylococcus toxoid in average doses of 1/100 unit, since bacterial immunity is usually low in these cases.

Sublingual Administration. Any of the above agents may be administered by the sublingual route using, as a rule, a dosage about ten times stronger than the injectible. The material is prepared in serial dilutions containing 50 per cent glycerine. This therapy may be used as an adjunct or alternative to injections. Doses must be given from one to three times daily depending upon the allergen employed. Pollens must be given about every six to eight hours. Food drops are administered about 30 to 45 minutes before each ingestion. Various oleoresins such as those from various plants may be introduced by the sublingual route.

SECONDARY FACTORS IN THERAPY

Before the introduction of optimal dosage therapy an adequate clinical history, physical and laboratory examination must be made in order to establish more accurately a definitive diagnosis. All factors which appear to contribute to the cause of symptoms should, if possible, be eliminated or avoided.

Secondary factors or a multiplicity of etiologic agents may be involved. For example, food and dust sensitivities are common in hay fever. Food and drug sensitivities may complicate inhalant allergy. As a rule, optimal doses are usually smaller in these complicated cases, especially in hay fever.

Optimal dosage therapy may precede, accompany or follow the use of ACTH and the corticosteroids. Other hormonal factors may be important such as the thyroid, estrogens and androgens. Nutritional, psychosomatic and other factors which may affect the general health are also important.

Finally, certain drugs may be administered for symptomatic relief, such as ephedrine, aminophylline, the antihistamines, etc. Specific surgical procedures also may be indicated in selected cases.

Acute, subacute or chronic infections of the respiratory tract may complicate the picture.

SUMMARY

A general consideration of all the recent observations on the basic mechanism of allergy strongly suggests that enzymatic adaptation on the part of the body cells is the most logical explanation. Optimal dosage therapy represents a means of stimulating this basic mechanism to dispose of allergenic agents in such a manner that symptoms are either ameliorated or abolished. Especial caution is followed in avoiding overdosage and a disruption of the enzymatic system with the production of toxic proteolysis, allergic reactions and eventual cellular damage. The clinical application of this principle of therapy may be summarized as follows:

1. Optimal dosage therapy is based upon the principle of the parenteral administration of allergenic or antigenic agents in those minute doses and amounts which will produce a satisfactory physiologic or immunologic response.

2. Initial doses are based chiefly upon clinical standardization but in certain instances such as pollen therapy, for example, serial dilution titration testing may be of value.

3. The duration of effectiveness of individual doses vary from a few hours to several days, sometimes two or three weeks, depending upon the agent employed and the existing degree of hypersensitivity.

4. The optimal dosage method is safe and effective, the results are satisfactory and no untoward reactions of any type are likely to be encountered.

5. Allergenic agents other than those employed for parenteral administration such as foods, drugs and inhalants must be considered also in therapy.

6. Secondary factors as related to 1) hormonal agents such as ACTH corticosteroids, thyroid, estrogens and androgens, 2) psychosomatic problems, 3) nutrition, 4) infection and 5) general conditions, are also important in therapy.

634 NORTH GRAND AVE.

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LVII

THE PERIBASAL NOMOGRAPHIC TECHNIQUE OF STAPES MOBILIZATION

VICTOR GOODHILL, M.D.

LOS ANGELES, CALIF.

In previous publications our concern with the basic physiologic objective of stapes mobilization (stapedolysis) has been repeatedly stressed. The surgical objective of stapedolysis is adequate remobilization of the entire middle ear mechanism to again transmit undistorted auditory vibrations to the perilymph with essentially normal amplitude. Thus, one should achieve lysis of the ankylosed stapedial footplate in such a manner that the entire footplate or a movable fragment thereof will be in continuity with the intact mobile ossicular chain, either through one or both stapedial crura resulting therefore in either monopod or bipod stapedolysis.

THE FOOTPLATE APPROACH

There has been a significant evolution in the modus operandi of the surgical technique of stapes mobilization since the first publication of Rosen,[1] when he advised mobilizations via the stapedial neck with a specially curved instrument. Shortly thereafter, others[2] suggested force application through the lenticular process of the incus, through the capitulum of the stapes, and other modifications in the region of the incudostapedial joint. It was quite logical that initial attempts to mobilize the ankylosed stapedial footplate should begin at the incudostapedial joint, because of its anatomic accessibility and the possibility of transmitting force through stable crura.

However, it was noted that incudostapedial dislocations could be troublesome, and that crural fractures could be severe problems. In a large number of cases force applied to the joint itself could give a false sensation of mobilization which in fact was mobility due to crural trauma. In this group of patients, the stapedial footplate

From the Departments of Otolaryngology, University of Southern California School of Medicine and Cedars of Lebanon Hospital, and the Deafness Research Laboratory at Children's Hospital, Los Angeles. Presented before the Sixth International Congress of Otolaryngology, Washington, D. C., May, 1957.

remained ankylosed even though the stapes appeared to be mobile on digital palpation. This approach, coupled with nonquantitative, nonaudiometric evaluation of adequacy of the surgical procedure, was responsible for many failures.

The recognition of the importance of quantitative measurements, and the utilization of a mathematical formulation of surgical physiology through the audiometric nomograph technique pointed out some of these dangers due to inadequacies in surgical manipulation. This new attitude, coupled with better magnification and illumination of the fossa ovalis and stapedial crura, logically turned the attention of the otologic surgeon to the footplate region.

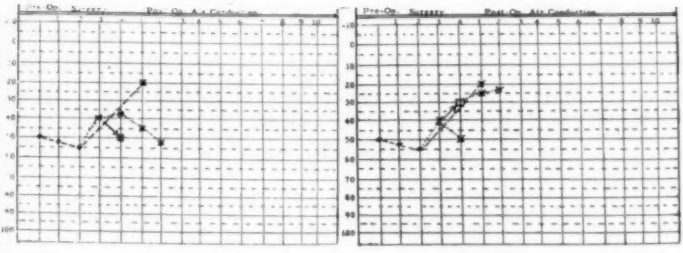
Footplate attacks have been quite varied, and have consisted of direct fractures, incisions, applications of hammer force, fenestration, and peripheral curettage of the footplate region. Each of these procedures has its advocates who ascribe special merit to one or another technique. In all of these footplate approaches, there has been one area of agreement, namely, that preliminary operative results are greatly improved in numbers and in magnitude of threshold shift.

The creation of a fenestra within the footplate either intentionally or unintentionally by either a crack or a burr-hole or a curetted area will result in an opening of the perilymph space of the vestibule to contact the tympanic air space. The exudation of perilymph through such a crack or fenestra will allow the formation of a pool of perilymph in the recessus ovalis. This pool will in effect represent a physiological continuum with the vestibular perilymph space. The square area of such a pool will be at least as large as that of the footplate, and will thus receive a large sound pressure as transmitted through the tympanic air space directly from the speaker's voice or from the audiometric receiver. Thus, a marked improvement in hearing will be realized in almost every case when the footplate is fenestrated (if no intravestibular lesion exists). With the drum open, such a gain in hearing will be almost comparable with the gain registered by a successful mobilization of the entire stapes in continuity with the ossicular chain and tympanic membrane. It has been claimed that the creation of such a fenestra in the footplate is indeed advantageous and it is recommended as a planned surgical procedure if the footplate cannot be adequately mobilized by pressure through the neck, with resultant crural fracture or incudostapedial dislocation.

My experiences in footplate fenestration have been unsatisfactory.[3,4] While it is true that temporary hearing gains usually occur

on the operating table, most of these gains are not maintained, and the vast majority show immediate or early closure. Furthermore, the gains in threshold obtained temporarily by this technique are significantly lower than those obtained primarily by physiologic monopod or bipod stapedolysis.

The utilization of the nomograph technique of surgical audiometry in stapedolysis has been described in detail elsewhere.[5] This technique offers a physiologic guide to stapedolysis surgery in terms of measurement of airbone gap closure and adequacy of force application. It also is informative in evaluation of the physiologic status



A B

Fig. 1.—*A.* Typical nomographic course in footplate fenestration (inadvertent). Drop at Step 4 with gelfoam typical of inadvertent footplate fenestration. Note poor nomographic response at Step 4 and early closure with loss of operative gain. Note additional drop at Step 4 when gelfoam applied (□). *B.* Nomographic evidence of footplate fenestra corrected by anterior crurotomy and monopod lysis. Note improvement in threshold at Step 3 followed by marked drop at Step 4. Re-inspection immediately revealed a solid fixed anterior crus and a footplate fracture. An anterior crurotomy and monopod lysis permitted ossicular continuity with the posterior footplate fragment and adequate lysis. Good result.

of tympanic structures. It is of value, moreover, in the differential diagnosis between a footplate fenestration and a true monopod or bipod stapedolysis procedure. The nomograph (Fig. 1A) technique calls for four operative steps: step (1) is made after preliminary elevation with the drum closed; step (2) is made with the drum open prior to mobilization; step (3) is made after a preliminary mobilization attempt; steps (3-A, 3-B, 3-C, etc.) are progressive steps following progressive mobilization attempts; step (4) is made post mobilization with the drum closed, and steps (4-A, 4-B, and 4-C) may be necessary in rare instances if inspection of the nomograph reveals a

discrepancy suggesting re-opening of the middle ear and re-assessing the status of the mobilization attempt.

In the event that the force has inadvertently produced a footplate fenestra with a perilymph pool, this will usually show up on the nomograph in the comparison of steps (3) and (4). In such a case, there will usually be a very adequate gain at (3), either directly on the predictive line or to its left. At step (4) with the drum closed, however, in such a footplate fenestra there may occur either an inadequate gain or an actual marked drop in hearing, as illustrated in Figure 1A and B. If there is an inadequate gain, a small piece of gelfoam is placed in the intercrural space. If such gelfoam packing

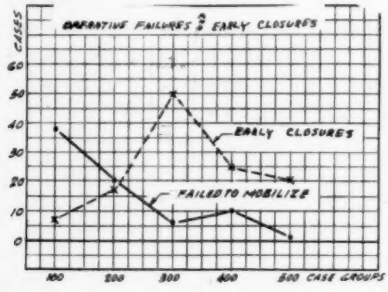


Fig. 2.—Operative Failures and Early Closures. In the case group between No. 300 and No. 350, attempt at improving results was made by intentional footplate fenestration. There was an immediate marked improvement in operative successes in which the number of cases which failed to mobilize dropped considerably. However, during this identical period, there was a very marked increase in early closures as noted in the dashed line above. When the peribasal approach was substituted for the footplate fenestration technique, the good immediate results persisted, but the early closures dropped drastically, thus indicating that footplate fenestration techniques were spurious surgical victories.

reverses the relationship and creates a normal rise at step (4), it will probably indicate that the footplate fenestra existed concomitantly with a mobile monopod or bipod stapedolysis. Should the footplate fenestra exist alone, the gelfoam pack will frequently produce a temporary drop in threshold at step (3) accompanied by a similar drop at step (4). Thus we see a diagnostic value of the nomograph in differentiation between a footplate fenestra and a mobile footplate or footplate fragment (monopod or bipod stapedolysis).

It may be of interest to observe the fate of a significant number of footplate fenestrations that were performed intentionally early in the course of my mobilization experiences. In 1955, a group of more than 50 patients were subjected to footplate fenestration in the hope that this would solve many of the previously insoluble problems. Operative (immediate) successes were indeed high, as indicated on the graph in Figure 2, but postoperative failures were extremely frequent and our over-all average of successes dropped to a very low level during this period. When the approach was redirected to the stapedial circumference and to the area of the stapedial ligament with avoidance of footplate fenestration, there was a marked increase in long range results.

Accordingly, it is my feeling today that in view of our present experience, the locus of choice for force application is the peribasal region, i.e., the circumferential or ligamentous area of the footplate in which the calcareous otosclerotic bridge is broken through, and in which attempts are made to preserve inviolate the integrity of the footplate itself without fenestrating it.

THE PERIBASAL TECHNIQUE

Details regarding anesthesia, canal incision, elevation of canal tympanic flap, and adequate exposure of the middle ear have been described in previous publications.[2] It is necessary to employ excellent illumination and magnification for the peribasal technique. This calls either for the use of the dissecting microscope or a combined loupe headlight combination with a magnification of at least 4x.

The incus is gently tested for mobility by palpation with a fine angulated needle probe engaged within the lenticular periosteum. Even in the presence of a rigidly ankylosed stapes, there is a degree of mobility of the incus which is easily determined by such palpation. If the incudomalleolar joint is fixed, as it may be, in congenital anomalies or adhesive otitis media, this diagnosis is all important. Such incudomalleolar fixation may well account by itself for the entire conductive loss, or on the other hand, it may co-exist with stapediovestibular fixation and cause failure if its presence is not realized.

The integrity of the incudostapedial joint is then assessed by palpation. A loose joint will call for extraordinary manipulation care to avoid incudostapedial dislocation.

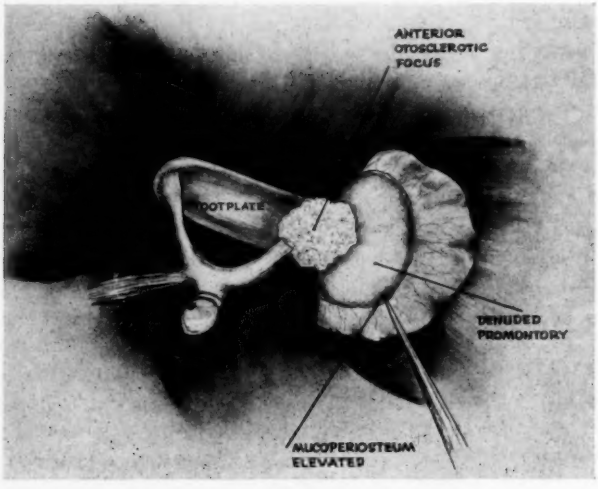


Fig. 3.—Peribasal Anterior Stripping.

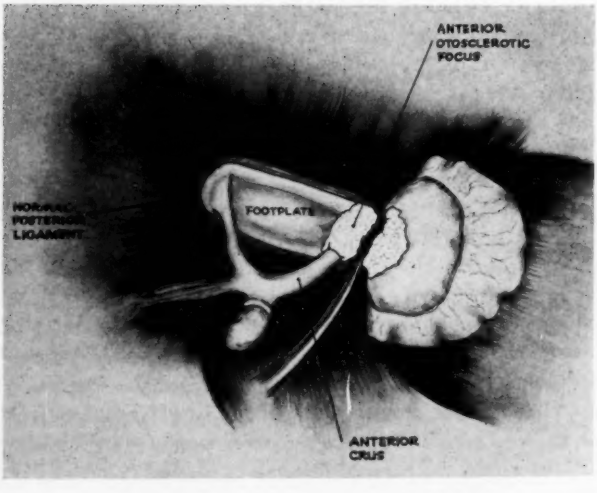


Fig. 4.—Peribasal Anterior Lysis (Bipod).

It has been our experience that safe transincudal or transcapitular force be used successfully in the relatively early or mild ankylosis states.

By no means can these types be predicted always from the threshold, age, or duration of disease. However, in many of the less mature forms of the disease, the ankylosis may be confined to the anterior limb of the footplate, or occasionally to the posterior limb alone. In such instances, safe lysis may be possible by force applied to the entire ossicular chain via the lenticular process or the capitulum or the neck.

Digital force is gentle but firm. During its application the entire ossicular chain must be observed as a total mechanism with special attention to the footplate region. In most successful cases there will be a general loosening and the stapes will usually be displaced slightly in a posterior direction. When effective displacement appears to have occurred, an audiometric test with nomograph guidance is obtained. Such alternations of force application and audiometric tests are used until a decision is reached.

At present, in most instances our approach is directly to the peribasal region, and not to the footplate per se. The first step is a careful survey of the footplate and contiguous areas. If such a study reveals, for example, an advanced invasion of the anterior crus and anterior limb of the footplate by the otosclerotic process, attempts at "bipodal" (two-legged) lysis are almost certainly doomed to failure. In such a case, the only hope of success is in "monopodal" (one-legged) lysis with anterior crurotomy. If, on the other hand, inspection reveals normal integrity of both crura but invasion of the footplate and ligament by otosclerotic bone, peribasal use of a needle probe can be highly successful and result in preservation of the anatomic continuity of both crura (bipodal) with a mobile footplate, a normal, and thus desirable, physiologic state. To achieve careful footplate lysis with attention to the above physiologic principles, force can be applied digitally with needle probes of varying sizes and angles, and tiny chisels; such instruments may also be used in severe ankylosis problems, in conjunction with the electric hammer, or microvibrator.

In using the peribasal technique to attempt a bipodal lysis, it is desirable (Fig. 3) first to strip the periosteum in the anterior peribasal region and then insert the needle probe (Fig. 4) immediately anterior to the anterior crus towards the vestibule through the region normally occupied by the annular ligament (which is frequently replaced by

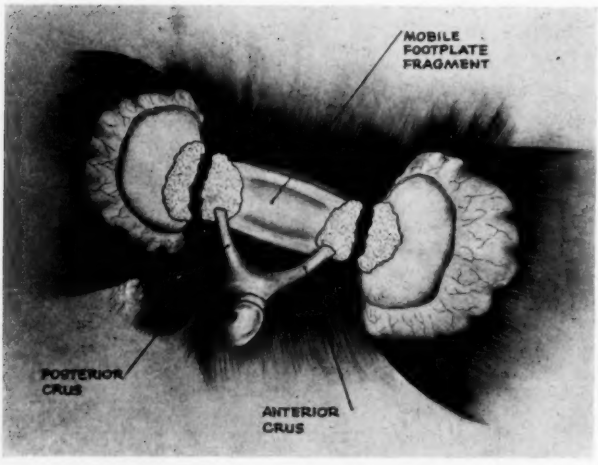


Fig. 5.—Peribasal Anterior-Posterior Bipod Lysis.

pathologic bone). If the disease is limited to the anterior limb, this maneuver alone may be adequate to produce lysis.

If adequate lysis is not demonstrated visually and confirmed nomographically the same procedure is carried out in the similar position posterior to the posterior crus (Fig. 5), again through the region of the annular ligament, since in such cases there will be lesion posteriorly as well as anteriorly.

If advanced extremely sclerotic lesions, usually in the anterior limb of the footplate, prevent successful peribasal penetration in this region and if inspection reveals reasonably free mobility at the posterior limb of the footplate, recourse to a monopod type (Fig. 6) of stapedolysis is possible through the procedure of anterior crurotomy similar to that advocated by Fowler.[6] In most of these cases the anterior crus will be quite atrophic as it approaches the neck region whereas the base of the anterior crus may be extremely sclerotic. It is possible to sever the anterior crus in the atrophic area quite simply with a sharp needle or an angulated knife. The use of a scissors is somewhat dangerous in that it tends to produce incudostapedial dislocation. Following anterior crurotomy, a fine needle or fine chisel is placed directly upon the footplate immediately posterior to the

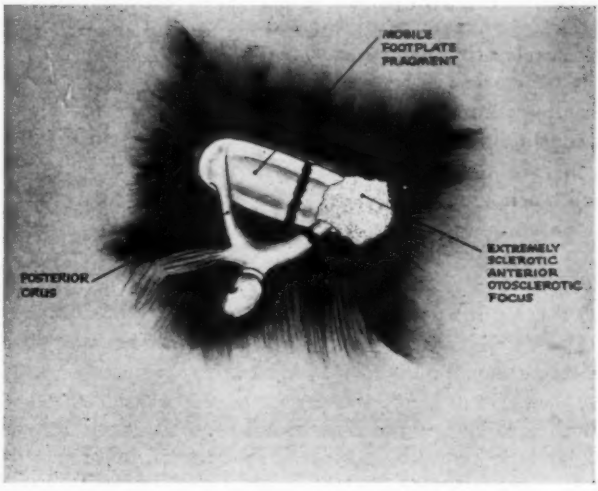


Fig. 6.—Posterior monopod lysis with anterior crural fracture and anterior footplate fracture.

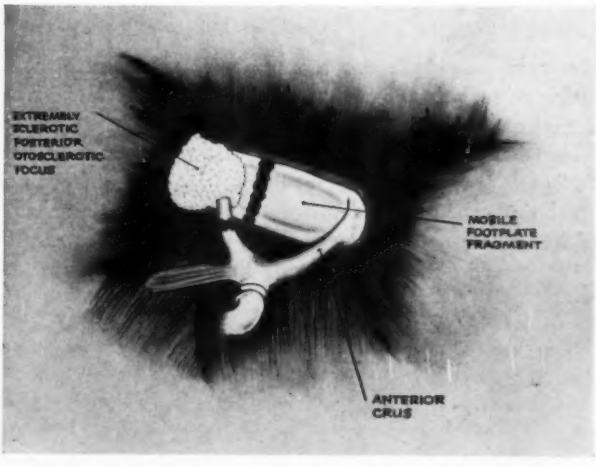


Fig. 7.—Anterior monopod lysis with posterior crural fracture and posterior footplate fracture.

otosclerotic lesion involving the anterior limb and penetration of the footplate proper is then accomplished, thus freeing the posterior crus and the posterior fragment of the footplate from its attachment to the fixed otosclerotic bony process.

This allows immediate mobility of the posterior footplate fragment in continuity with the posterior crus which in turn is in physiologic continuity with the ossicular chain. If this is carefully performed, such monopod lysis can be quite successful and has an excellent prognosis, almost as good as bipod lysis.

In very rare instances the same problem may occur in the reverse situation, that is, involving the posterior limb of the footplate. In such cases, a posterior crurotomy (Fig. 7) will be necessary allowing for an anterior monopod lysis.

If both anterior and posterior crural footplate angles are severely involved by otosclerotic bone, then stapes mobilization is a surgical impossibility and it is of no use to attempt any manipulations in this area. Such a condition immediately destroys the possibility of physiologic continuity between ossicular chain and footplate fragment. In such cases the only possibility of perilymph mobility restoration is through fenestration of the horizontal semicircular canal.

RESULTS

It is not the purpose of this communication to go into the subject of evaluation of techniques and statistical study of results. This is in itself a complex area of discussion. Such reports have been published recently elsewhere.[3] Suffice it to say, however, that in a study of almost 700 cases in which there has been a good deal of evolution of surgical technique the utilization of the peribasal technique has shown a marked improvement in primary postoperative results, resulting in the last 100 cases in the following findings:

A.	Successful results	62%
B.	Significant gains	29%
C.	Failures	9%

As previously stated, our concept of surgical success involves dual criteria: a) closure of the air bone gap, b) achievement of the 30 decibel practical hearing level. Most successes qualify in both cate-

gories. A small number of patients with poor bone conduction levels qualify only in closure of air-bone gap for obvious reasons. These are primary results, it must be emphasized. Long range results present an entirely separate statistical problem which is now being evaluated.

SUMMARY AND CONCLUSIONS

1. The surgical objective of adequate lysis of the ankylosed stapedial footplate requires remobilization of the entire middle ear mechanism to again transmit undistorted auditory vibrations to the perilymph with essentially normal amplitude.

2. This objective can best be accomplished by a monitored surgical technique employing surgical audiometry with mathematical guidance through the nomograph technique.

3. Avoidance of incudostapedial dislocation and crural trauma requires the utilization of the peribasal technique in the majority of cases.

4. Simple fenestration of the footplate yielded poor postoperative results in our experience.

5. It must be emphasized that long range results in stapes mobilization surgery may seriously change the present primary postoperative statistics. Such long range studies are now in process.

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LVIII

MALIGNANT TUMORS OF PARANASAL SINUSES TREATMENT AND RESULTS

W. H. Struben

Amsterdam, Netherlands

The subject of malignant tumors is as important to the general practitioner as it is to the specialist. Patients with malignant processes are nearly always seen by the specialist at a later time than by the practitioner.

For that reason the general practitioner can be of great help to the specialist by giving him information about the earliest symptoms. He is the most important link between patient and diagnosis. If he suspects malignancy he will advise the patient on the time factor and choice of clinic and specialist. Another reason is that in cases of malignant growths there will often be a moment when the specialist will refrain from further treatment as no improvement is to be expected, or the patient himself may discontinue all treatment. It is at this time that the patient or his family will insist on his going home, on leaving the hospital and passing the last part of his life among his family or in their direct neighborhood. Then the general practitioner takes over again, if not for treatment then for advice on nursing. So it seems that in a civilized world we all start and finish our life under medical superivsion.

I will refrain from speaking about the complicated anatomy of the paranasal sinuses. It is clear to all of us that as the nose and sinuses are all covered by the same type of mucous membrane and are all related to each other by an opening into the nose, it is also easy for a tumor to spread from one sinus to another by way of the natural openings or per continuitatem.

A survey made of cases treated in the Netherlands Cancer Institute in Amsterdam between 1942 and 1955 shows several interesting facts. Not all cases have been taken into consideration but only those of which all facts are known. Many had to be omitted as those

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Read at the Sixth International Congress of Otolaryngology, Washington, D. C., May 1957.

patients were deported during the war, or died in concentration camps. The patients who were initially treated elsewhere (in a different clinic) have also been omitted.

Eighty-five patients form the basis of this investigation. Sixty-one male patients at an average age of 61.5 years and 24 female patients at an average age of 61.6 years were treated. In 35 patients the tumor was situated on the right side and in 50 patients on the left side.

As in all cases of malignant tumors, there is too long a lapse of time between the first symptoms and the final diagnosis. The average time lost was seven months, the shortest time being six weeks, the longest four years. This seems incomprehensible but we should remember that all symptoms of a malignant disease of the nasal sinuses are in no way different from those of benign processes like sinusitis. A physician or a specialist who is not daily confronted with malignant tumors will naturally rather think about the more common possibilities than of a tumor. Only they who are connected with cancer institutes or a clinic where much work is done on cancer patients will have a more suspicious nature. They also know, however, that the patients who are sent to their clinic are already more or less selected cases. You will now understand that, without being able to blame anyone, a very long time may pass between the first symptoms and the time a definite diagnosis is made. This time-lag has, however, very great consequences, for it means that in nearly all cases which came to our clinic more than one sinus was involved.

There is only one sure way to diagnose a malignant process, and that is by taking a biopsy and obtaining the pathologist's opinion. If the diagnosis is made we like to know the extent of the tumor for three reasons: firstly, the radiologist needs to know the exact outline of the tumor as he wants the whole tumor in his field of radiation. This is necessary, so he can be sure that the outer part of the tumor will also get the full dose of radiation. Secondly, the surgeon wants to be sure that during operation he will not at any stage unknowingly cut through the tumor. Thirdly, if we do not know more or less the exact extent of the tumor it will be very difficult to decide if a certain case is operable or not. It is also of great importance for the prognosis. Those cases where x-rays show infiltration in or destruction of the bony parts of the base of the skull and naturally those with distant metastases are to be considered inoperable. I regret to say that even with the help of an x-ray examination, stereoscopic x-ray and

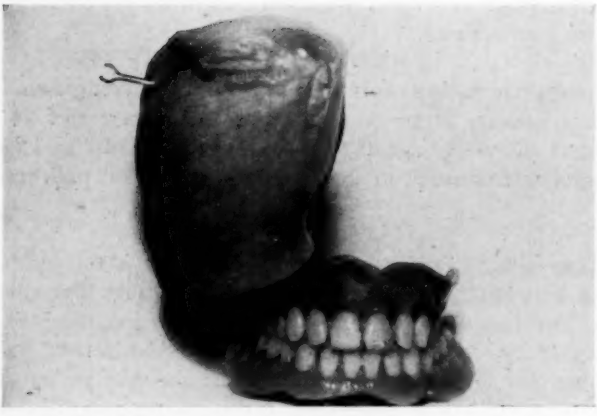

Figure 1

planigraphy, it is not always possible to get the definite localization of the tumor but we keep on improving our results by combined operation. Those tumors extending into the pterygopalatine fossa are specially difficult to evaluate.

As with nearly all malignant processes we have the choice between radiology, surgery and combined treatment. Radiology means x-ray or radium treatment. Surgery may be done by the knife or by diathermy and in the case of combined treatment a choice can be made between, first, surgery and then radiology or, first, radiology and then surgery.

Those who advocate surgery first insist that it is much easier to recognize the difference between tumor and normal tissue when there has been no radiation previous to operation. Others are of the opinion that by giving radiation before operation most of the tumors become smaller in size and therefore become better operable. It was our experience in cases treated first by radiation and then by operation: that there was no difficulty in recognizing the outline of the tumor, that there is no more appreciable bleeding and that there is certainly less chance for metastases even if a part of the tumor is cut through accidentally. Whatever combination one chooses, one will have to wait two or three weeks before starting the second part of the treatment, being it radiology or surgery.

Figure 2

Figure 3

TUMOURS OF PARANASAL SINUSES
NETHERLANDS CANCER INSTITUTE.
1942 — 1955.

♂	♀	R	L
61	24	35	50

TABLE I

We have tried several combinations of treatment, because we are still trying to improve our results, as we are not contented with the percentage of the five-years results.

All our operations have been done by diathermy except when we were sure to be far outside the tumor and planned to close the wound or parts of it after operation. It is interesting to note that radical or nonradical operations, followed by radium, did not differ much in the five-years results. Nonradical operation was only performed when the tumor seemed to be too extensive for a radical operation. But if we look at Table III and Table IV it is obvious that radical and nonradical operations differ clearly in some respects.

Roentgen-radiation before operation and roentgen-radiation alone gave very disappointing results.

In Table III you will find that in cases of first operation and then radium, about 50 per cent of the patients died of cancer. This percentage is less in cases treated first by x-rays followed by surgery; it is 80 per cent for cases treated by x-rays alone. But if we look at the average survival time of the patients, then we see that those treated by radical surgery followed by radium therapy have a far better prognosis and that those treated by radiation (x-rays) followed by

TUMOURS OF PARANASAL SINUSES
NETHERLANDS CANCER INSTITUTE
1942 — 1955.

	TOTAL	†	2 YEARS	5 YEARS	%
Diath.(radical op.)+Ra.	20	17	11	5	25%
Diath.(non-radical op.)+Ra	21	18	7	4	19%
Rö+Diath.(radical op.)	18	14	5	—	
Rö	21	20	3	1	±5%
Diath.(non-radical op.)+Rö	3	3	—	—	
Diath.(non radical op.)	2	2	—	—	

TABLE II

surgery show the poorest results; even if there are fewer cases who died from tumor.

This might suggest that radiation by deep x-rays in these cases is a far heavier burden for the patient than radiation by radium or because radium was always given after operation and deep x-rays before operation, it might mean that in these latter cases the products of cell destruction did not have sufficient drainage and therefore the patients might become more toxic. The reason that fewer patients died from tumor in the group treated by x-rays followed by surgery is seemingly because they lived a much shorter time after initial treatment.

Table IV gives the number of local recurrences and metastases and we find that radical operation is no insurance against local recurrence nor metastases but there is a very great improvement in the average time it takes before a recurrence or metastases occur. It is also understandable that the number of recurrences and metastases is higher in the group of radical operation followed by radium because the average survival time is longer.

We see less recurrences and metastases by roentgen treatment followed by diathermy, a finding that is probably attributed to the

TUMOURS OF PARANASAL SINUSES
NETHERLANDS CANCER INSTITUTE.
1942 — 1955.

	Total	†	† from tumour	%	average survival time after treatment
Dioth.(radical op.)+Ro	20	17	10	50-%	32.75 months
Dioth.(non-radical op.)+Ro	21	18	11	52.3"	23.22 months
Rö+Dioth.(radical oper.)	18	14	8	42.2"	9.25 months
Rö	21	20	16	76.2"	15.38 months
Dioth.(non radical op.)+Ro	3	3	2		
Dioth.(non radical op.)	2	2	1		

TABLE III

fact that a lot of these patients die after a short time before there is a chance to develop recurrences or metastases (Table III).

Most of the tumors were squamous cell carcinoma; 67 out of 85. This has also been mentioned by others. Interesting is the fact that the results of the anaplastic tumors or undifferentiated squamous cell carcinoma or sarcoma are much better than we should expect. These are supposed to be very radiosensitive, but normally they develop early recurrences and distant metastases (Table V).

CONCLUSIONS

1. We should try to diminish the time between onset of the first symptoms and definite diagnosis; here the general practitioner could be of great help.

2. Combined treatment is the treatment of choice except in cases of anaplastic tumors.

3. Radical surgery followed by radium gave the best results.

4. The pathology of the tumor does not give sufficient insight into the results or prognosis.

TUMOURS OF PARANASAL SINUSES.
NETHERLANDS CANCER INSTITUTE
1942–1955

	Total	†	local recurrences	average time	metast.	average time
Diath.(radical oper.)+Ro.	20	17	18	19.7 months	5	22.4 months
Diath.(non radical oper.)+Ro.	21	18	11	9.– months	6	2. months
Rö+Diath.(radical oper.)	18	14	6	7.8 months	3	on admittence
Rö	21	20	13	5.7 months	5	3.2 months
Diath.(non radical oper.)+Rö	3	3	1	lived less than 1 year		
Diath.(non radical oper.)	2	2	0	lived less than 1 year		

TABLE IV

No patient has been rejected for operation on account of his age or general condition but we have in all cases waited for permission from the Department of Internal Medicine. In our Institute a very close co-operation exists between the internal medicine, surgery, ear-nose-and-throat and radiology departments which is essential for good results. Every patient who is brought into the clinic is examined by the department of internal medicine. Decision on treatment is taken in a combined session three times weekly.

The entrance through the palatine fossa and palate will be insufficient in most cases. We use this approach only in cases of maxillary antrum tumors localized at the floor of the antrum; for tumors situated or originating in the ethmoid region we use the paranasal approach and for tumors which involve more than one sinus we like to enter through the orbit if this is involved or go through the cheek if the lateral wall of the maxillary antrum is destroyed.

It is without doubt a greater mutilation but to our regret we found out that one cannot compromise in cases of malignant tumors. It is of the greatest importance to have as wide a field of vision as possible.

If the tumor has broken anywhere through the bony wall of the orbit, the eye should be removed even if the patient has no complaints

TUMOURS OF PARANASAL SINUSES
NETHERLANDS CANCER INSTITUTE.
1942—1955.

	Total	2 years	4 years	5 years
Squamous cell carcinoma	67	19		9
sarcoma or undifferentiated squamous cell carc.	7	4	2	
chondrosarcoma	1			1
cylindroma	4	2		
adenocarcinoma	5			
osteogenic sarcoma	1	1		

TABLE V

about his eye or vision. It is sometimes difficult to have definite preoperative proof if the tumor has involved the orbit and for that reason the surgeon should always ask permission to remove the eye if during operation it should become clear that this is necessary. We have never seen anything but disaster if you leave an eye in when the tumor has invaded the orbit. It should not be forgotten that the patient with a malignant tumor has but one chance to survive and that is at the first radical operation.

We should also bear in mind that we are treating human beings and every patient as well as every tumor is behaving differently. Even if we are speaking about certain forms of treatment one never can generalize in treating malignant tumors. A certain tumor will behave in a different way in two patients, it even may behave differently in two places in the same patients. To get the best results we should know every thing about the tumor, its behavior, its biological form and we should know everything about the patient.

The most important question before we start any treatment at all is the question whether we can improve the situation of the patient or not. His age, his occupation, the extension and the nature of the tumor, they all come into consideration.

Metastases of tumors of the paranasal sinuses occur, to our knowledge, late and mostly in those cases where repeated operations on the primary tumor have been done. They can be found in the cervical glands and as distant metastases in the lung. An x-ray of the lungs of every patient is taken as soon as he or she is admitted to the hospital. In cases where metastases in the cervical glands exist at the time when the patient comes under treatment, we treat the primary tumor first and as soon as there is a reasonable certainty that the primary tumor is under control, we follow with a neck dissection. We never practice preventive neck dissection if no glands are palpable at the start of the treatment.

It is unnecessary to perform a neck dissection as a preventive measure because very often no metastases do occur, and our own and others' experiences show that it is still safe to do a neck dissection as soon as pathological glands appear. This means, however, that there should be a regular and very careful follow-up of patients with malignant tumors.

Rehabilitation is very important for patients who have undergone large operations on the face for malignant tumors. With the help of a dentist we have always made a mold of the upper and, if necessary, of the lower jaw before the operation. In this way we have a provisional denture or plate ready at the operation, as in many cases part of the palate and alveolar process has to be taken away. We are then able to put the denture in at the end of the operation; this has several advantages:

The patient is able to speak, drink and eat and secondly we have a good support for our dressing; it keeps the dressing clean and very little food or drink enters the wound. This provisional plate or denture is easily corrected if it might become necessary to take out some more tissue at a later date or if sequesters come out after the operation. No permanent denture is made before we are reasonably sure that all tumor has been removed (Figs. 1, 2 and 3).

The same procedure is used for a facial defect. We have never been tempted to do a plastic operation and I would like to repeat the words of Sir Stanford Cade who once told me: "No plastic surgeon should be allowed in the neighborhood of a patient with a malignant tumor." Even if you do not agree with this in general it is certain that where a plastic surgeon has to use a knife and plastic operations

generally take several months and sometimes even more than a year, the chance that sooner or later the surgeon might cut into a recurrence of the tumor is great. This will be disastrous. Furthermore, after closing the cavity, inspection will be difficult or impossible, while with a facial plate inspection is easy.

The end results with a facial plate are not quite the same as those after a plastic opertion but to our opinion fair enough, and very much sooner obtained and a lot cheaper. It is easy to rehabilitate the patient in this way and it should be done as soon as possible so that he can start his work as a normal human being.

1 VIOTTA ST.

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LIX

THE MECHANISM OF HEARING LOSS IN EARLY CASES OF ENDOLYMPHATIC HYDROPS

JUERGEN TONNDORF

IOWA CITY, IOWA

The term "Ménière's disease" is generally used to describe a clinical entity of vertiginous spells, tinnitus and deafness. The tinnitus and deafness are usually unilateral. The hearing loss, in the words of Williams,[16] "exhibits a tendency for greater interference with the transmission of low tones than high (ones). . . . A characteristic feature of the deafness, at least in the early stages of Ménière's disease, is its tendency to increase and decrease, seemingly in a capricious manner." This low-tone fluctuating deafness a) invariably involves the threshold for both air and bone-conducted sound; b) displays recruitment in the affected ear;[6] c) commonly is associated with diplacusis, in most cases the pitch being perceived higher in the affected ear;[14] d) shows a marked lowering of threshold for aural harmonics;[12] and lastly e) displays a loss for speech intelligibility disproportionally large in comparison to the loss for pure tones.[6]

The etiology of the disease is not completely understood at present. However, in 1938 Hallpike and Cairns[7] reported on the histological examination of two cases. They described a condition which has become known since as "endolymphatic hydrops," a dilatation of the endolymphatic space, mainly in the region of the cochlea and the saccule. Subsequently, these findings have been confirmed by a series of additional case reports.[8-10,13,18]

Attempts have been made to explain the hearing loss on the basis of the hydrops phenomenon. Mygind,[11] for instance, suggested that the stapes might be fixed by the increased labyrinthine pressure from within thus hindering transmission of vibratory energy. Bekesy,[3]

This research was supported in part by the United States Air Force under contract number AF 41(657)-148, monitored by the School of Aviation Medicine, USAF, Randolph Air Force Base, Texas. Read at the Sixth International Congress of Otolaryngology, Washington, D. C., May 1957.

however, was able to demonstrate experimentally that transmission of sound via the stapes is not noticeably affected by an increase in labyrinthine pressure. Yet the type of deafness incurred (limited to low tones and fluctuating) does not favor the assumption of cochlear (haircell) pathology as its main underlying cause. Actual cochlear pathology, which has been observed histologically, is more likely to be a sequela of the hydrops and may account for the permanent relatively flat or often greater loss for high frequencies usually found in the later stages of the disease. Hence speculation should once more be focused upon the possibility of a mechanical impairment of sound transmission induced by the hydrops. This hypothesis has been advanced by Lindsay at several occasions.[9,10,17]

The rationale for the above may be supported as follows. A distention of the endolymphatic duct stretches its membranous boundaries. Reissner's membrane, because of its lesser stiffness, bulges out considerably, whereas the displacement of the basilar membrane, because of its greater stiffness, is probably so small that it escapes detection in histological examinations. Bekesy[2] has measured the elastic properties of the basilar membrane. In its normal state, it does not possess any tension. Its stiffness is not uniform but varies over its length in an exponential manner; the value at the basilar end being about 100 times greater than at the apical end. These elastic properties of the basilar membrane favor the formation of traveling waves along this membrane.[4,5] The traveling waves were first observed by Bekesy in 1928.[1] It is now recognized that they form the essential link in the transmission of vibratory energy from the stapes footplate to the basilar membrane on its way to the organ of Corti.

It was proposed, therefore, that the alteration of the elastic properties of the cochlear partition, due to the distention of the membranes, might affect the pattern of traveling waves within the cochlea. If found correct, this might offer an explanation for the type of hearing loss incurred in early cases of endolymphatic hydrops. To study this problem, model experimentation seemed best suited.

PROCEDURE

Throughout the following, anatomical names will be used for the corresponding parts of the model. This does not imply that the structures so named are the physical equal of their namesake in each and every respect. A cochlear model, constructed after Bekesy,[1] had been used in other experiments reported elsewhere.[15] The frequency

response of this model, in terms of demonstrable traveling waves along the basilar membrane, extended from approximately 10 cps up to 500 cps. This downward shift of the frequency range is explained[1] by the fivefold enlargement of the model over the dimensions of the human cochlea. Incorporated into this model was a cochlear duct for purposes of the present experiments. A schematic picture of the modified model is shown in Figure 1. In some experiments a different arrangement was used in that Reissner's membrane was made to run parallel to the plane of the basilar membrane instead of being set at an angle. The two membranes were made of rubber cement, a technique formerly used by Bekesy. This permits production of thin membranes for the sake of greatest sensitivity and to simulate the

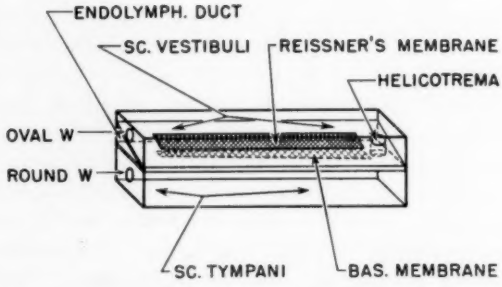


Fig. 1.—Cochlear model (schematic) after Bekesy's[1]; five times natural size. Present model contains a cochlear duct with Reissner's and the basilar membrane set at an angle. A loud speaker driver unit (not shown) was directly coupled to the oval window for vibratory stimulation. The manometric device by means of which the endolymphatic pressure was varied is not shown either.

stiffness gradient of the basilar membrane to some extent. Reissner's membrane was made uniformly stiff. The stiffness ratio between the basilar membrane, in its most yielding (apical) section, and Reissner's membrane was approximately 1:2 which probably falls short of the actual ratio by a wide margin. To use basilar membranes of greater over-all stiffness (in an effort to improve this ratio) was inadvisable as this reduced the sensitivity of the model beyond the limits of convenient observation. Thinner membranes of Reissner were used occasionally for the purpose of quick orientation. Actual measurements were not feasible with such thin membranes as they invariably leaked, which of course defeated the purpose of the present experiments. Threfore the above mentioned stiffness ratio of 1:2 between the two

membranes had to be accepted. Glycerin-water solutions of varying viscosities were used for both the peri- and the endolymphatic fluids. Membranes were kept functional in these solutions for days and sometimes for weeks so that a variety of measurements was conducted on one set of membranes. This made comparison of the results from different experiments more reliable.

The cochlear duct was connected to a ½ cc tuberculin syringe with a small manometer in parallel. No. 160 polyethelene tubing, which offered an appreciable resistance to the flow of fluids in the range of viscosities employed, was used for all connections. To assure immediate indication at the manometer of pressure changes within the endolymphatic duct, the lines from the syringe to the manometer and to the endolymphatic duct were made equally long. The endolymphatic duct contained 500 cu mm at what might be termed the resting pressure and the manometer permitted differential readings at 8.5 cu mm intervals. Hence it was feasible to alter the pressure (and the volume) within the endolymphatic duct in calibrated minimal steps of 1.7 per cent of the resting pressure. Since for small increments volume and pressure alter in exact proportions, these terms may be used interchangeably. The manometer of course registered only pressure changes.

Both the oval and the round window were made of condom rubber. Vibratory stimulation of the model was provided by a loudspeaker driver unit which was connected directly to the oval window by means of a small air filled, closed coupler. An actual stapes was not present. Since interest was only in the assessment of relative changes, a psychophysical method was used. The just noticeable (jn) motion of the membranes, etc., was assessed by an observer under standard conditions of illumination and microscopic observation. The results were recorded in terms of the voltage readings across the driver unit. This method had given satisfactory results in previous studies.[15]

Illumination was either by stroboscopic or by continuous light. Stroboscopic light served to slow down the membrane motion for observation of the wave pattern, whereas continuous light was used for demonstration of "eddy" pathways or of the orbits of particle motion within the fluids.

RESULTS

The events induced by changes in the endolymphatic pressure will now be reported. When the endolymphatic fluid volume was

increased both Reissner's and the basilar membrane showed its maximal distention in its center section because of its uniform stiffness and fixation at both endpoints. The basilar membrane formed its maximal distention near its distal end where stiffness was least. (The end itself was fixed to the frame.) The distention per unit distance was reciprocally related to stiffness which as stated earlier varied in an exponential manner. In fact, the shape of the bulge gave visible evidence of the exact form of the stiffness gradient. The form of the bulge is shown in Figure 2. Needless to say there was a proportional increase of the bulging of both membranes with each increment of the endolymphatic fluid volume. When the endolymphatic fluid volume was decreased below its resting value both membranes bulged in; the shape of both bulges being exactly the same as upon volume increases except for the change in direction.

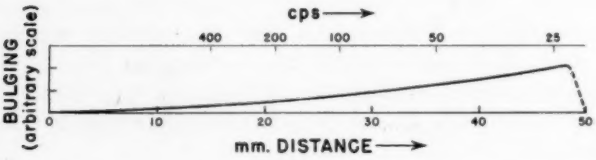


Fig. 2.—Bulging of the basilar membrane per unit distance in response to increased endolymphatic pressure. Graph was obtained by gradually increasing the pressure and noting the visible extent of the bulge at each level. The location of maximal displacement amplitudes for several frequencies (under the condition of resting pressure) is indicated along the upper rim.

The frequency response curve of the model was now determined, in terms of the jn membrane motion in response to each frequency, with the endolymphatic fluid volume at its resting value. When this initial response curve was taken as reference and the endolymphatic pressure increased in discrete steps, the sensitivity of the model was altered as is shown in Figure 3. The loss in sensitivity increased with each incremental step of the endolymphatic fluid volume and was in some reciprocal relation to frequency. Since the loss is plotted in log (db) steps as is the frequency, the actual relations are best approximated by a family of e-functions (of the general form $y = 1 - e^{-ax}$) running asymptomatically against the zero-db line.

Three pieces of evidence point to the cause of the observed loss in sensitivity of the membrane response. 1) If the results presented in Figure 3 are compared to Figure 2 it is apparent that the loss per

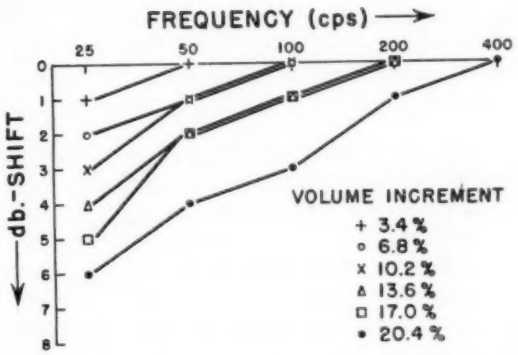


Fig. 3.—Loss in sensitivity of basilar membrane displacement per frequency upon increase in endolymphatic fluid volume (figures of the parameter express changes in volume per cent).

frequency is proportional to the distention of that section of the basilar membrane in which the maximal amplitude of displacement is formed for that particular frequency. 2) Results similar to those presented in Figure 3 were obtained when the stiffness of a single cochlear partition (basilar membrane only) was increased by adding extra coats of rubber cement to the membrane. After each additional coating the loss curve was determined and found to increase. This procedure was limited to a total of three coatings by the fact that each new coat partially dissolved the old membrane. It became lumpy in spots which disturbed the smooth gradient of stiffness. 3) The results presented in Figure 3 were obtained upon an increase as well as upon a decrease in endolymphatic pressure. It is therefore evident that the loss in sensitivity is brought about by an alteration of the elastic properties of the basilar membrane, to wit by putting the membrane under tension. Quantitatively, the loss per frequency is proportional to the degree of tension added and reciprocally related to the original stiffness of each section of the membrane within which the maximal amplitude of displacement is located.

No attention was paid in preparation of Figure 3 to the exact location at which the maximal amplitude was formed, while the tension of the membrane was altered. Figure 4 shows a gradual shift of this location for five test-frequencies plotted against the increment of the endolymphatic fluid volume. The shift is in a general proximal direction, i.e. toward the location of higher frequencies, and more so

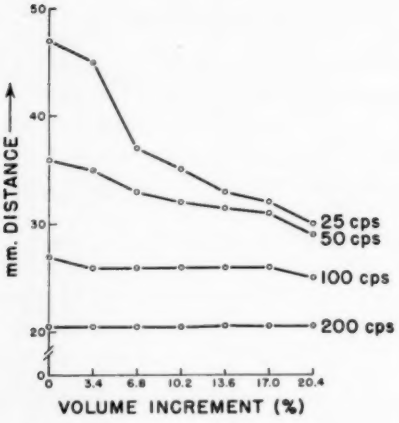


Fig. 4.—Shift of the location of maximal displacement of amplitude of the basilar membrane for five frequencies (25-400 cps) upon increases in endolymphatic fluid volume (in per cent of the resting value).

for low than for high frequencies. Assumption seems plausible that the cause underlying this shift is the same as that just explained for the case of the sensitivity loss: the added tension of each section of the basilar membrane in relation to its original stiffness.

It is customary to describe the traveling event along the basilar membrane by its envelope. By this term is meant a line which "envelops" all points of displacement of the traveling bulge at all times. The finding of the shift of the location of maximal amplitude, as shown in Figure 4, indicated that the entire envelope pattern might change under the effect of altered endolymphatic pressure. The pattern of the envelope was ascertained by the following method. First, the location of maximal amplitude for a given frequency was assessed by the method of jn motion. Thereafter, stimulus intensity was increased by 3 db, 6 db, 10 db and 15 db and the visible extent of the envelope determined at each of these levels. Plotting the results as distance along the membrane vs. (linear) amplitude rendered a graphic representation of the particular envelope. Then, the endolymphatic pressure was increased and the procedure repeated at each new pressure level. A representative set of curves for a frequency of 50 cps is given in Figure 5. The asymmetrical pattern of the master envelope is noted. The curves pertaining to higher pressure levels were obtained by a geometric reduction of the master curve.

The measured values fitted this family of curves to a satisfactory degree. They definitely did not fit curves obtained by arithmetic reduction of the master curve. These results indicate that the envelope, in addition to the proximal shift of its maximum, gradually loses its asymmetry when the basilar membrane is put under tension.

Suspension in the perilymphatic fluids of finely grained metallic particles, such as aluminum powder, are used for demonstration of Bekesy's "eddies" and also for that of particle motion within these fluids. The general pattern of both of these events along a single cochlear partition (basilar membrane only) is shown in Figure 6 for the case of one of the perilymphatic scalae. (The events within the other scala are completely symmetrical, only of opposite direction with reference to the basilar membrane.) The eddy occurs in the region

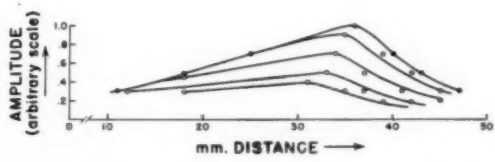


Fig. 5.—Envelopes over the displacement pattern of the basilar membrane. Curve with solid dots pertains to endolymphatic pressure at rest (Master curve). Curves pertaining to increases in endolymphatic pressure (values as indicated) were obtained by geometric reduction of the master curve. Open circles represent the measured results.

of the maximal amplitude of membrane displacement. Its path follows the proximo-distal direction of wave travel along the membrane with the return flow taking place along the outer wall. Particle motion, synchronized with the impressed frequency, is longitudinal at the proximal end but gradually becomes trochoidal (of the elliptical variety) along the membrane. In the region of maximal membrane displacement, this AC particle motion becomes superimposed upon the DC eddy motion. Further details (part of which are indicated in Figure 6) need not be discussed here as they are unessential for the present case. Interested readers are referred to the original publication[15] from which Figure 6 was taken.

Next, the effect was studied of alteration of the endolymphatic fluid pressure upon eddy and particle motion. To this end, the pressure was altered repeatedly between extreme values and at a relatively fast rate so that changes became immediately noticeable which were

then recorded. Eddy motion was seen to spread more distally in spite of the fact that the location of the amplitude maximum simultaneously moved in a proximal direction (Fig. 4). In response to low frequencies (below 50 cps) rather complex eddies are normally formed around and through the helicotrema. These eddies were found to speed up under the effect of altered endolymphatic pressure, a definite sign of the spreading of eddy motion in a distal direction. However, when a small section of the eddy was observed under the microscope and the endolymphatic pressure altered, the velocity within this section was seen to slow down. In other words, the eddy became broader and less distinct. Likewise, particle motion, upon alteration of the endolymphatic pressure was seen to extend farther distally

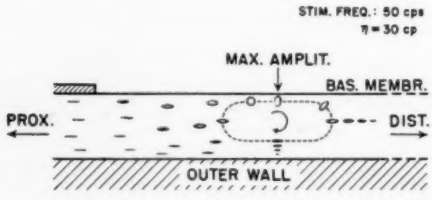


Fig. 6.—Patterns of Bekesy's eddy and of particle orbits in one perilymphatic scala along a single cochlear partition (basilar membrane only). Both the "eddy" and the particles revolve in the direction of the arrow. Note the decrease of particle amplitude of membrane displacement as indicated.[15]

than is indicated in Figure 6. However, the orbits of individual particles became elongated indicating a relative lessening of their transversal amplitude (Fig. 6). Both of these observations (concerning eddy and particle motion) show that by putting the membranes under tension less energy is expended in a transverse direction across the cochlear partition. Instead energy travels farther distally to be expended partly by equalization via the helicotrema and partly by frictional damping. The latter is the major means of energy dissipation within the cochlea, according to Zwislocki's mathematical considerations.[19] The mode of alteration of the envelope pattern under the effect of increased endolymphatic pressure (Fig. 5) is now understood to be caused also by the distal spreading of the traveling energy. For this reason, the curves in Figure 5 were represented better by a geometric reduction of the master curve than by an arithmetric one.

Marked alteration of the endolymphatic pressure had a curious effect upon the shape of the particle orbits, a detail which has been

neglected in the description so far. The orbits became kidney-shaped instead of their (normal) elliptical configuration. This became noticeable mainly in the immediate vicinity of the basilar membrane. Such orbits are shown in a schematic manner in Figure 7. It is apparent that the orbits faced the basilar membrane with their concave side when the pressure increased, and reversed their position when the pressure decreased. This difference in behavior was the only one noted between the effects of positive and negative changes of endolymphatic pressures.

How and why these kidney-shaped orbits come about is best understood from consideration of the nature of the (ordinary) elliptical orbits. Such an orbit is shown in the insert of Figure 8. They result, like Lissajou figures, from the interaction of two vectorial forces; in this specific case by the (forced) movement of the oval

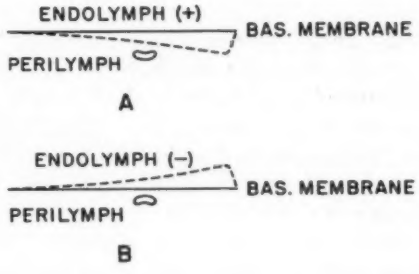


Fig. 7.—Particle orbits in response to pure-tone stimulation upon marked alterations of endolymphatic pressure (schematic). A) endolymphatic pressure increase; B) endolymphatic pressure decrease.

window and by the (induced) movement of the cochlear partition. The phase difference between these two vectors is exactly 90° as attested by the complete symmetry of the orbits. There is only one place (cf. Figure 6: tilting orbit in upper right position where the "eddy" leaves the membrane) at which this 90° phase difference is temporarily lessened.[15] Of course, it is altered also when the membrane is not perpendicular to the direction of the driving force (i.e. the window movement). This occurs whenever the membrane, under the effect of altered endolymphatic pressure, bulges out or in. In this case the long axes of orbits in the immediate vicinity of the membrane follow the tilt of the membrane.

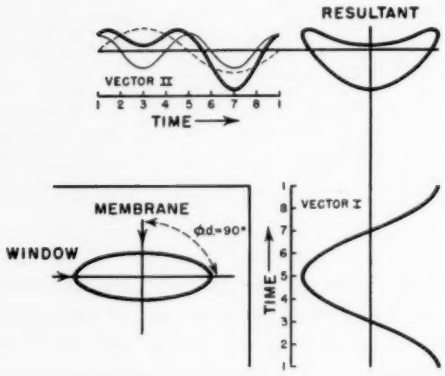


Fig. 8.—Graphic analysis of a Lissajou figure resulting from harmonic distortion of one of its vectors. Present are the fundamental and 2nd harmonics.

After this digression, discussion will be continued of the problem posed by the phenomenon shown in Figure 7. Analysis of Lissajou figures can be performed graphically or their pattern can be reconstructed with the aid of an oscilloscope. Graphic analysis of the pattern in Figure 7 is executed in the main drawing of Figure 8. The principle is as follows: Combination of vector I and II obtains the resultant by plotting the displacement amplitudes at corresponding time points together in a two-dimensional manner. Conversely, when one vector (i.e. vector I) and the resultant are known vector II can be reconstructed along its own time scale. The pattern of vector II in Figure 8 is recognized as a complex wave form consisting of the original frequency (vector I) and its second harmonic. The phase relation between both component frequencies is indicated in the drawing. For other phase relations, resultants of different orientation will obtain as might easily be understood from consideration of Figure 8. Actually the drawing of Figure 8 represents a slight simplification of facts. This becomes obvious when one compares the Lissajou patterns of Figures 7 and 8. The drawing in Figure 8 is composed of the first and second harmonics, where as the actual particle orbits in Figure 7 contained higher harmonics as well. If a fourth harmonic is added to vector II of Figure 8, the resultant Lissajou figure would more nearly attain a true kidney shape.

The two patterns of Figure 7 must be recognized as resulting from harmonic distortion; the difference between pattern 7A and 7B

being explained as a phase inversion of the newly added second harmonic. Other harmonics might be present also but escaped attention because of their relative smallness. This distortion must have been introduced by the membrane movement, since it was not present in the original stimulus (i.e. in vector I). The latter can be stated with certainty for two reasons: 1) the pattern of orbits in response to complex stimulation (combination of first and second harmonic) are characteristic double-looped Lissajou figures,[15] which are easily distinguished from the present pattern; 2) such double-looped orbits display the phase relation between the component frequencies of the stimulus. A change of this phase relation, such as that from Figure 7A to Figure 7B, does not occur, unless the stimulus pattern itself is altered.[15]

This is not the first observation of nonlinear distortion occurring in a cochlear model. Another observation concerned the reproduction along the cochlear partition of the pattern of a beat frequency[15] which instruments reacting linearly never show. For the present case, the following explanation is offered. Harmonic distortion is known to occur in mechanical, vibrating systems when the elastic limit of the system is exceeded. This occurs whenever the stimulus intensity becomes excessively high. The range between the resting position of the elastic element (the "operating point") and the elastic limit is termed the dynamic range of the system. When a membrane is put under tension, the dynamic range is lessened and distortion must occur at relatively lower stimulus intensities. Actually the system executes vibrations by swinging in both directions around its operating point. Thus there are two elastic limits, one positive and the other negative. Hence when the membrane is distended under the effect of a one-sided pressure, as in the present case, the operating point is shifted causing an asymmetry of the elastic properties of the system. In this latter case distortion occurs also and the phase relation between the original frequency and the added harmonic(s) is inverted whenever the direction of the distending force is reversed (Fig. 7).

ADDITIONAL OBSERVATIONS

The results reported in the following have no direct bearing upon the question at hand; however, they are felt to have importance for the basic problem of cochlear mechanics.

Figure 9 shows the alteration of the eddy pattern induced by the incorporation of the cochlear duct. Both eddies are perfectly sym-

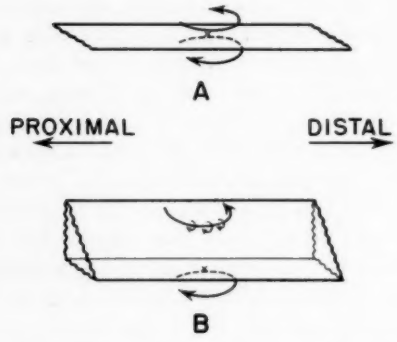


Fig. 9.—A. Symmetrical pair of eddies on both sides of a single cochlear partition. The (x) marks the location of maximal displacement amplitude. The actual membrane is not shown. B. Eddy pattern along both sides of a cochlear duct with Reissner's and the basilar membrane set at an angle to each other.

metrical (Fig. 9A) along a single partition (basilar membrane only). (The same symmetry was found when the two membranes were running parallel to each other.) When the membranes were set at an angle (Fig. 9B) the eddy in the vestibular scala became complex. It revolved in two planes instead of one; the plane of the added component being perpendicular to that of the original one and transverse to the long cochlear axis. The diameter of the new transverse component varied with the amplitude of membrane displacement. The direction of flow was from the lower toward the higher side of Reissner's membrane and the return flow along the outer wall. How is this direction to be explained? Bekesy[4] found that wave travel along the basilar membrane invariably follows the direction from greater to lesser stiffness. That the eddy sweeps along the membrane in the same direction (Fig. 9A) has already been stated. A similar mechanism may be operative in the transverse component of the eddy along Reissner's membrane. Hence the stiffness along the low side of Reissner's membrane ought to be greater than along the high side. This may actually be the case if one assumes that the stiffness of the basilar membrane is "looking" through Reissner's membrane in a reciprocal relation to the distance between both membranes. The plane of particle motion was not altered by the additional eddy component.

Glycerin-water solutions of varying viscosities were used as labyrinthine fluids, as has already been mentioned. It had been found in

previous experiments[15] that alteration of viscosity of the perilymphatic fluids affected the damping within the model. The sensitivity of the membrane was lowered, the distal slope of the envelope steepened, and the DC eddy current slowed down in proportion to the increase in viscosity. When damping was very low (viscosity smaller than 10 centipoises [cp]) a secondary train of waves appeared to originate at the distal end of the membrane traveling in opposite direction to the original one, i.e. in a proximal direction. Such wave travel toward the source had been termed paradoxical wave motion by Bekesy.[4] In the model cited it had been caused by the fact that close to its distal point of fixation the stiffness gradient of the membrane is reversed, an unavoidable by-product of the mode of production of these membranes. It was quite possible, therefore, that the damping of the present model might be influenced by the ratio of viscosities between the endo- and perilymphatic fluids. To answer this question, the wave pattern in response in various frequencies was observed with the viscosity of the perilymphatic fluids constant at 30 cp, while that of the endolymphatic fluid was altered in steps. The above hypothesis was generally confirmed. Specifically, when the viscosity ratio was much smaller than 1 marked paradoxical wave motion was seen and interfered with observation of the ordinary (proximodistal) wave trains. This was made worse by the fact that the distal slope of the envelope became less steep. For this reason, all observations reported above, in reference to Figures 3-5, had been made with a viscosity ratio of approximately 30 (endolymph: 1000 cp; perilymph: 30 cp). A value of 30 cp for perilymphatic fluids has previously been found as representative of the damping conditions within the human cochlea.[15]

Another variable to be explored was the stiffness ratio between the basilar and Reissner's membrane. This ratio had to be made quite small for experimental reasons as explained above. The distribution of frequency maxima along the cochlear partition had previously[15] been found to depend upon the value of the stiffness gradient: the smaller the gradient, the wider the distance between maxima for given frequency intervals. A single cochlear partition (basilar membrane only) had displayed maxima 4 mm apart for intervals of one octave, and this distance between maxima had been maintained practically over the total frequency range of the model. After a Reissner's membrane of uniform stiffness had been added, the distribution of frequency maxima became wider and was no longer linear for octave intervals (Fig. 4). This finding may be explained by the fact that the stiffness gradient for both membranes combined is different from

that of the basilar membrane alone, especially in view of the relatively great stiffness of Reissner's membrane. The change in stiffness must affect the distal portions of the cochlear partition more than the proximal ones and therefore spread the distance between maxima of low frequencies more than for high frequencies. This is confirmed by the result presented in Figure 4.

A final remark: a few experiments were conducted, while a perilymphatic pressure outlet was present simulating the cochlear aqueduct. It consisted of a short piece of narrow tubing leading out from the basal end of the tympanic scala and allowing equalization of DC pressure changes within the perilymphatic space. Opening of this outlet did not visibly affect any of the phenomena reported in this paper.

COMMENT

In a more recent article Bekesy[5] reported upon some effects induced by alterations of the elastic properties of the basilar membrane. A cochlear model was made to behave according to any of the major hearing theories by simply altering the over-all stiffness, the stiffness gradient, the transverse tension, and the coupling between its parts. The findings reported here result from a still different form of change: the introduction of an over-all tension by distending the membrane.

The problem posed at the outset was that of finding an explanation for the type of hearing loss incurred in early endolymphatic hydrops. The seven characteristic signs were cited as follows: 1) hearing loss more pronounced for low than for high frequencies; 2) equal loss for air and bone conducted sound; 3) fluctuation of loss; 4) recruitment; 5) diplacusis; 6) lowered threshold for aural harmonics; and 7) disproportional loss for speech intelligibility. Of these, the equal loss for air and bone conducted sound is explained by the fact that the locus of impairment lies beyond the stapes footplate. Two others, recruitment and the speech perception loss, can hardly be expected to result from an alteration of sound transmission within the perilymphatic fluids. The observed fluctuation of the loss is best accounted for by the assumption of a varying endolymphatic pressure. The three remaining ones (the dominance of the hearing loss in the low-frequency region, diplacusis, and the lowering of the threshold for aural harmonics) are paralleled by appropriate findings within the model. The observation occasionally reported of diplacusis as a down-

ward shift of pitch in the affected ear cannot be explained at the present. However, concurrence in the five points listed permit establishment of a rational basis for the characteristic type of hearing loss in early cases of endolymphatic hydrops. Whether the opposite occurrence, a shrinking of the endolymphatic space, as suggested by the experimental findings, is a clinical possibility cannot be decided at present.

A few words of caution might be in order here. Firstly, the so-far unexplained occurrence of recruitment and of the speech perception loss suggests the possibility of a concomitant temporary impairment of haircell function. Recruitment, generally accepted as a sign of cochlear impairment at the haircell level, is not necessarily a permanent acquisition. Temporary hearing losses due to noise are accompanied as a rule by recruitment which disappears as the hearing recovers.

Secondly, application of the findings reported in this paper must be limited to the phenomena as such. Quantitative correlations between experimental and clinical data cannot be established. For that the model is still too crude a replica of the cochlea. Based upon present information, the amount of increased endolymphatic fluid volume necessary to induce a given threshold shift is open to conjecture. However, Bekesy's detailed correlations between his findings in cochlear models and later observations in actual cochleae permit considerable confidence in the general information derived from this type of model experimentation.

Lastly, some observations reported in the foregoing concerned effects which were induced by the presence of Reissner's membrane, such as the complex "eddy" (Fig. 9B) and the nonlinear distribution of frequency maxima along the basilar membrane (Figs. 2 and 4). These phenomena were largely due to experimental imperfections of the present model, i.e. to the relatively great stiffness of Reissner's membrane. The distribution of frequency maxima measured in a human cochlea is a linear function of distance along the basilar membrane over the major portion of the frequency range (Bekesy[3]) and is obviously not affected by the added stiffness of Reissner's membrane. However, it must be pointed out again that even a very low value of stiffness of Reissner's membrane does not prevent the distention of the basilar membrane under the effect of altered endolymphatic pressure. It will only lessen its degree.

SUMMARY

Experiments were conducted on a cochlear model in an effort to find an explanation for the type of hearing loss incurred in the early stages of endolymphatic hydrops. Such models, upon increase in endolymphatic pressure, displayed:

1. A loss in sensitivity;

2. A shift of the location of maximal displacement amplitude along the cochlear partition toward the base of the cochlea; (both of the phenomena were more pronounced for low than for high frequencies);

3. Harmonic distortion.

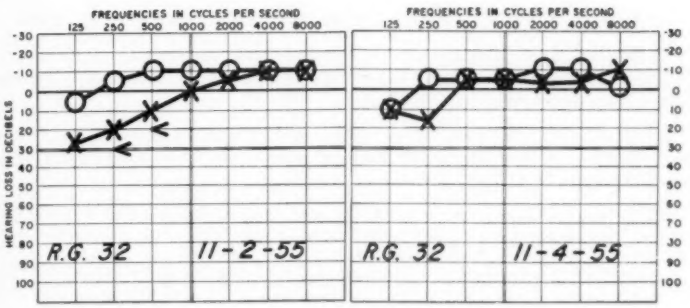
These observations are paralleled by clinical findings which are generally accepted as being characteristic of endolymphatic hydrops: hearing loss predominantly for low tones; diplacusis; and lowering of the threshold for aural harmonics. Recruitment and the disproportionally large speech perception loss which also are observed clinically cannot be explained on the basis of the present experimental data.

The changes observed in the model were caused by the increased tension of the basilar membrane under the effect of altered endolymphatic pressure. Several additional observations are reported also which are of a more theoretical interest for the general concept of cochlear mechanics.

UNIVERSITY HOSPITALS

When this paper was first submitted for publication, inclusion of an actual clinical case was felt unnecessary. However, in discussions concerning the findings reported here, the term "early cases of labyrinthine hydrops" was repeatedly misunderstood and in need of further specific definition. A brief description of a representative case therefore is appended.

The case concerns a 32 year old physician who at the time of his illness happened to be a resident at the Department of Otolaryngology, University Hospitals in Iowa City. Reliable audiograms for purposes of comparison were available antedating the onset of the illness by about one year. Dr. R. G. fell ill on November 1, 1955, with a sudden attack of moderate vertigo and a roaring-type of tinnitus in his left ear. He also noted some impairment of hearing acuity in the same ear. The



following day (November 2) he was able to submit to an audiometric test, the symptoms having somewhat abated over night. Two days later (November 4), the hearing had returned to approximately where it had been before the onset of the illness. Recruitment was never present as tested with the aid of a Bekesy audiometer. Slight diplacusis was noted on November 2 for some of the lower frequencies when presented to both ears simultaneously. No attempt of a quantitative assessment was made at that time. The threshold of harmonic distortion was not assessed either.

This attack was the first one the patient had ever experienced and as far as is known at present the only one so far. Other details of the history and findings do not concern the point in question and need not be reported here.

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Scientific Papers of the American Laryngological Association

LX

ADDRESS OF THE PRESIDENT

LeRoy A. Schall, M.D.

Boston, Mass.

Members of the American Laryngological Association and Guests:

As President of your Association, I have the honor to bid you welcome to the 78th annual meeting and to extend to you an invitation to participate in the discussion of the scientific papers that will be presented for your consideration.

May I express to the Association my appreciation for the honor that you have bestowed upon me. To be enrolled in the company of distinguished men and to serve as your president is indeed a great privilege and a great honor.

To the hard-working secretary, we owe an excellent program. To the vice-presidents, to the editor, to the treasurer, to the members of the council, I am indeed indebted for their guidance and support.

Dr. Nathan M. Pusey, president of Harvard University, in submitting his 1955-1956 annual report to the members of the Board of Overseers, stated that he assigned to himself the reading of the 130 Presidential Reports preceding his own and that from this experience he gained a strong feeling of kinship with his predecessors.

As president of the American Laryngological Association, I could do no less than follow the example set by the president of Harvard University. The reading of the presidential addresses of my predecessors has been an exhilarating and stimulating experience. My predecessors to this office were great men. They were pioneers, they

were master crafsmen, scientific observers and stimulating teachers. Their presidential addresses to this association show great literary skill, are of real historical value and create, in one, a true sense of humility in attempting to address you.

In the reading of their works, we learn of the struggles, of the fears, of the aims, and of the hopes of those leaders and pioneers of yesteryear. Many of the problems of our predecessors are still with us, only in different forms. We no longer debate whether one should spend five years or ten years in general practice before specializing. We no longer believe "the best men are not entering the specialty." From my many years of association with the American Board of Otolaryngology, I know that the basic training in otolaryngology has been improved. From my contacts with the candidates for their examination, I sincerely believe that excellent men are entering the specialty of otolaryngology.

Through the efforts of the Residency Review Committee, a committee composed of representation of the Board of Otolaryngology, of the Council on Medical Education of the American Medical Association and of the College of Surgeons, only those residencies that are 36 months in duration, and give a broad and thorough training, are approved for residency training in otolaryngology.

The exception to these requirements is that one of these years may be spent in a surgical residency.

In the early days of the American Board of Otolaryngology, special emphasis was placed on the value of histopathology in the education of the otolaryngologist. Those of us who have examined for the American Board know that the teaching of histopathology has been greatly improved in our institutions.

Next, special emphasis was placed on the basic sciences and, although it was never recorded as a requirement, it was generally recognized that an academic year spent in the study of the basic sciences was desirable. This feeling was so generally accepted that many of our teaching institutions started a basic science course lasting an academic year. Those of us who have had experience in postgraduate education know only too well that an academic year was much too long and that the curriculum would have to be padded.

With the returning war veterans with their GI bill, these courses were oversubscribed and they fulfilled a useful function. However, as time ran out, applicants for these courses became fewer and fewer and most of the courses have been abandoned. It is now generally recognized that the proper place for the teaching of basic sciences is concurrently with the residency training program. When a young man in the third or fourth year at medical school comes to you as head of your department and tells you that he is interested in otolaryngology and asks your advice as to the best road to specialization, what do you tell him? An internship of at least a year is a must, much better if it is two years. And then what? Shall it be a residency in pathology, a residency in medicine, a rotating service, a year in surgery or is he now ready after internship to accept a three-year residency in otolaryngoolgy? In discussing this problem with my residents, I find that the answer depends entirely upon the type of training that that young man has had. If he spent a year in medicine, he is convinced that a year in medicine after internship is excellent training. If he has spent a year in pathology, he, too, is just as certain that it is of great value to him. And those who have spent a year in surgery insist that that is the proper way to enter otolaryngology. Frankly, I do not know. As I watch their work in the wards, in the operating room, in the handling of patients, I have come to the conclusion that there is something besides the science of medicine that enters into the making of a successful physician.

I have been impressed by those young men who have had some general practice and know something of the art of handling patients and their problems. The art of medicine is not the sole property of any one discipline. There is something inherent in the soul that makes a man stand out above his brother. And I wonder whether or not we are playing fair and if we are not trying to shift our own responsibilities if we now demand that our residents receive part of their training under another discipline. Our predecessors were individualists. I would regret to see all of the future otolaryngologists cast from the same mold. I would like to see some room for individuality, as I firmly believe that there are many roads that lead to the making of a good physician.

Education is a continuous process. It must not stop at graduation. A three-year residency in otolaryngology is only a basic foun-

dation on which to build. As one's interest develops, additional time should be spent in special fields of endeavor, whether these fields be in otology, plastic surgery or research, in the field of broncho-esophagology or of malignant disease. To this end we offer to certain selected young residents a fourth, fifth and even a sixth year of specialized training.

Since the foundation of the American Board of Otoloryngology shortly after World War I, it has been the constant aim to improve the training in otolaryngology and to secure for the young men entering the specialty a good basic training. We confess that many times we have done that which we ought not to have done and have not done that which we ought to have done. I wish some one could answer the question as to why it is that only in the United States does the feeling prevail that the otolaryngologist does not measure up to his brother practiioner? This feeling does not exist in any other country that I have visited and I have visited quite a few.

During a professional career that is rapidly drawing to a close, I have never detected a feeling of superiority by those with whom I have been associated. My associates tell me that this has been their experience. I firmly believe that we as otolaryngologists, if you will permit me to quote an oft-quoted phrase, "have nothing to fear but fear itself."

In a few days there will be a meeting of the Sixth International Congress of Otolaryngology. This is the first time that it has been held in the United States and we are very proud to be hosts to our colleagues from overseas. Medicine is a common meeting ground for all races and for all creeds. We as physicians can play an important role in developing mutual understanding and respect for those of different races and of different creeds.

General Alfred M. Gunther, former Supreme Allied Commander in Europe and now president of the National Red Cross, stated in the New York Times of March 6 that "the United States needs some sort of a Medical Foreign Service or program for medicine in diplomacy and that the medical profession can play a tremendous role in building international understanding, as human misery is the same everywhere in the world." Let us then be good hosts to our brother

physicians from overseas, for I see no hope in this troubled world if the physicians of the world cannot live together in peace and in good will.

And may I say a word in behalf of our foreign medical students. Everyone of you is aware that during the Second World War and the Korean "incident," just recently declared a war, the demands of our military services depleted the ranks of our residents and interns. Had it not been for the doctors from foreign countries many of our hospitals could not have rendered their proper service to the sick. I would like to pay a tribute to these young men. I am proud of the fact that we have had residents, not only from our neighbors to the North and to the South, but from the East and from the West. All but two have returend to their native countries and there they are carrying on the practice of medicine in the American tradition. I know that their countries and their patients are grateful.

243 CHARLES ST.

LXI

SOME UNSOLVED PROBLEMS IN AVIATION OTOLARYNGOLOGY

Col. Paul A. Campbell, USAF (MC)

Washington, D.C.

During World War II it was my good fortune to appear before several of the members of this group with a paper concerning the problems of aviation otolaryngology at that time. It was most fortunate that considerable interest was generated and as a consequence a number of this group were very helpful. Some made very definite contributions. There are also a number of the organization who, while in the service of the Army, Navy or Air Corps made history in aviation otolaryngology.

The major problems at that time were protection against noise, communication in noise, aero-otitis media, aerosinusitis, selection criteria relative to the ear and vestibular apparatus, orientation and air sickness.[1]

These problems are in varying degree still with us; however, their relative magnitudes and their order of research priority, have changed considerably. In some instances, as is true in the noise problem, an entirely different population is affected.

Aviation, as you well know, has undergone vast changes since World War II. Altitudes achieved have increased by a factor of more than two; speeds have increased by a factor of more than three; noise levels have increased considerably; and, now to some extent at least, we have a new noise source, the transonic boom. We are reaching levels of noise which cannot be measured in decibels but must be measured in terms of atmospheres of pressure. Thus, we must now pause, review, and reinstrument to measure pressures which resemble rapidly repeating blasts.

It appears that almost every aspect of aviation is increasing expotentially. Almost every parameter, if plotted chronologically, has

followed an expotential curve. At present, more than 751,000 persons are employed in the aviation industry. Domestic airline traffic is now approaching a rate of nearly 43,000,000 paid fares per annum. International travel on aircraft from the United States is operating at a rate of more than 3,000,000 paid fares per annum. I believe we all recognize that aviation is rapidly becoming the most popular mode of medium range and long range travel in spite of the fact that the birth of aviation occurred only slightly more than half a century ago.

Cabin pressurization has solved many of the problems such as aero-otitis media and aero-sinusitis; although, we are all seeing cases from time to time. Both of the conditions are now beginning to be seen, to some extent at least, in their chronic forms especially among those who fly as an occupation. Chronic thickening of the tympanic membrane and dome-like elevations resulting from submucosal hemorrhages into the mucous membranes of the sinuses are not uncommon findings among flying personnel with many operational hours. Cabin pressurization has enabled most aircraft to fly in the still air above the weather and above the turbulent atmosphere associated with heat convection. This, and the more effective air sickness drugs, seem to have decreased the problem of air sickness. From the standpoint of most conditions, it now seems that almost anyone can fly who can get himself up the ramp onto the modern airliners.

Of interest, while on the subject of aircraft cabin pressurization, are a few statistics of one of the largest airlines of this country. These statistics compare incidence experience before the advent of pressurization and that at present with pressurization. They are shown in Table I.

TABLE I

NUMBER OF CASES PER THOUSAND PASSENGERS CARRIED

CONDITION	BEFORE PRESSURIZATION	AFTER PRESSURIZATION
Ear Discomfort	0.8	0.2
Air Sickness	3.0	0.65
Oxygen Want	1.0	0.1

Noise as a problem is still quite a serious one. Many of us in the aviation business wish it could be quietly charmed away but it can't.

Each advance in aviation and each innovation seems to be plagued with more and more noise and the quality of the noise seems to annoy more people.

Most of this problem resolves itself into the situation that noise seems to be an inescapable byproduct of the types and amounts of energy used in aviation and the ways they are applied. Noise, however, is wasted energy and performs no function necessary to flight. In fact, it affects materiel as well as personnel. Thus, aircraft structures and airborne equipment are adversely affected by it. The problem is a very broad one and the energies involved seem to outrun our abilities to cope with them.

In the past few years the human side of the problem has changed greatly in that those most affected are maintenance personnel rather than pilot and passengers. The noisiest aircraft while on the ground often become reasonably quiet in the air.

Protection by means of ear defenders, puffs or helmets of the individual who maintains aircraft, is reaching a point of diminishing returns as weight and bulk of the protecting material interferes with work efficiency as well as comfort. Placing the individual in a soundproofed capsule decreases his ability to maneuver and use his tools. It is only a partial answer.

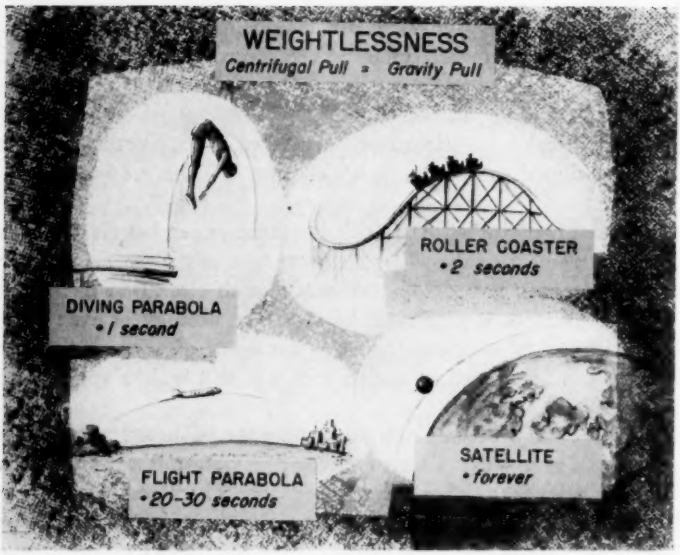
A great deal of effort is now being expended toward fundamental studies of the very basic aspects of the problem—that is basic studies of noise production, noise sources and the media through which the energy is transmitted. Thus research emphasis is being transferred from the receiver to the transmitter. Many fundamental studies are being performed on the changes in noise produced by jet stream alteration. The term noise cancellation technique, wherein the negative phase of the propagated wave is used to cancel out the positive phase, is being heard more and more often in engineering discourse. Electronic propagation of out-of-phase wave sources to cancel out extraneous wave sources, are considered. Methods by which noise can be converted into useful energy receive a great deal of attention.

In the past year personnel protection through selection, assignment and periodic recheck has received increased impetus through

more careful and more complete study of those being subjected to sound of high energy. In the United States Air Force, through official regulation, those individuals working in areas in which sound energies are sufficient to be damaging are given frequent audiometric study. If they show changes in their audiograms which indicate possible damage they are studied from the standpoint of vulnerability, and if they cannot be adequately protected from further changes they are reassigned to an area in which they will be protected.

In spite of all the effort which has been expended on the noise problem, it seems that it will take some entirely new principle or technique to solve the problem. Whether such a solution lies within the realm of physics, engineering, bioacoustics, otology or even pharmacology, it will be welcomed when it comes. I assure you that any help which can be offered by such a group as this will be appreciated.

Now, let us proceed from the problems of today to those of tomorrow and even a day after tomorrow. Aviation is now approaching a new phase, flight above the atmosphere where resistance of the medium in which flight takes place ceases to be a factor and when, given sufficient speed, a vehicle can orbit the earth more or less forever without further expenditure of energy unless, of course, it is struck by some object such as a meteor or meteorite of sufficient mass to alter its trajectory or velocity. Changes in course or return to earth will require some use of energy but as long as it orbits above the atmosphere, there will be no expenditure of energy. The satellite of the International Geophysical Year will be the first example of a man-made orbital vehicle. As orbiting represents an exact state of equilibrium between centrifugal force and gravitational pull, the vehicle and all objects on board will be in the gravity free state or in other words, weightless. With man in the gravity free state, there will be many problems. This group will be interested in the problem resulting from the effect on orientation when the gravity vector is absent, as it will be in the gravity free state. We all agree to some extent at least with the basic concept of the equilibration triad and that the three elements are the visual apparatus, the vestibular apparatus and the kinesthetic pparatus. I believe we also agree that two of the functions of the equilibration triad must be present if we are to have efficient balance and orientation. Our problem stems from the fact that two of the elements of the triad seem to depend on gravity as a moment



METHODS OF PRODUCING WEIGHTLESSNESS

Fig. 1.—At the top of a diving parabola a body experiences weightlessness (Zero "g") for a period of fractions of a second. The "Zoom" at the top of a roller coaster arc may produce weightlessness for a period up to two seconds. Flying a parabolic course at high speeds may result in periods as long as 30 seconds. A satellite vehicle above the atmosphere remains weightless.

of force. These, of course, are the otolithic portion of the vestibular apparatus and the kinesthetic apparatus. The question then is: what will be the effect on orientation if the gravity vector is absent?

To date, no one has developed a laboratory situation which will produce the gravity free state for more than a second or so. By flying the so-called Keplarian parabolic course, weightlessness has been produced for periods up to something in the neighborhood of 30 seconds. Individuals who have had this experience in the Gerathewohl[2] studies at the USAF School of Aviation Medicine fall into three

categories: those who enjoyed the strange situation and felt they were not adversely affected, those more or less indifferent, and those who were disoriented and became ill. The problem will be resolved only when we can get people into the situation for long periods of time (Fig. 1). It is of interest to mention here that many gravity substitutes such as acceleration and deceleration, either linear or tangential, have been suggested. These, however, require energy expenditure.

Now to the final category of problems of this discussion and one which I believe falls into the broad interests of this organization—the problem is reconstruction or simulation of the atmosphere. At altitudes in the region of 70,000 to 80,000 feet, compression of the thinning outside atmosphere into the cabin becomes uneconomical because of the weight of the compressor. At about these levels, a completely sealed cabin is required and man must carry along with him the constituents of the breathing air he must have. For weight economy he must use over and over again the exhaled products. Thus, carbon dioxide must be broken down into carbon and oxygen. The exhaled air must be washed of its impurities and have its water vapor removed. This must be done at the least possible weight cost as weight is always a limiting factor in flight. Among other questions which then arise is the question of an ideal breathing gas. Should it be constituted just as that at sea level? Should some of the nitrogen be removed from it? Should it contain some helium from the standpoint of middle ear and sinus ventilation? or what?

Should we ever have a manned orbital vehicle in space, how can we within our weight restrictions, reproduce an atmosphere which on our planet earth requires a delicate symbiotic relationship between chlorophyl containing plants and the carbon dioxide producers of which man is one.

I know I have raised many questions and have answered a very few. Research for the flights of the future must broaden its base to involve more disciplines as many of the ideas and problem solutions will have to come from interdisciplinary studies and from groups such as this who at this time probably consider themselves more or less remote from the problems of future flight.

FOURTEENTH AND CONSTITUTION STS.

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LXII

HOMESPUN LARYNGOLOGY

LYMAN G. RICHARDS, M.D.

CAMBRIDGE, MASSACHUSETTS

A traveler returning from a far country was once questioned by his compatriots as to what had occasioned him the greatest difficulty on his journey. Had it, they asked, been the formidable mountains which had barred his way or the raging rivers which he had been forced to cross? Thoughtfully he replied that the element which had most sorely tried him had been the sand in his shoes.

Many patients who seek help from the laryngologist might metaphorically be said to constitute the "sand in his shoes." These patients present symptoms and complaints unassociated with any visible underlying pathology and lacking the interest and fascination of more obvious abnormalities. A partial list of these complaints to which I am sure you could all make your personal additions, would run as follows: a burning or choking sensation, a feeling of tightness, dryness, or itching in the nose or throat, a sense of irritation, rawness or bad taste in the mouth, a dropping in the back of the throat, a stuffiness in the nose, and that bete noire of every rhinologist, "sinus, doctor."

These and similar symptoms, bulking large in daily office practice, form a background or fabric through which run the admittedly more colorful, more medically challenging and more cleanly cut pathological entities which interlace it much as a few brightly hued threads might vivify a piece of homespun cloth. Hence my designation of this segment of our specialty as Homespun Laryngology.

Such symptoms and complaints have various characteristics in common. By and large they are essentially subjective and are unaccompanied by any consistent clinical or organic picture with which they can be dependably associated. They stand on no such demonstrable pathological ground as does hoarseness due to a vocal cord

tumor, nasal obstruction due to a large polyp, dysphagia occasioned by a retropharyngeal swelling or a purulent nasal discharge accompanying a maxillary sinusitis. One must accept the patient's estimate of his complaint as to location, mode of onset, lateralization, intermittancy, and severity. Indeed even the patient is frequently vague in his account of these details, thus leaving the physician without a satisfying guide toward a diagnostic goal.

It is not, I think, any reflection on a doctor's enthusiasm for his work if he finds that a visible mass in the nasopharynx of a patient complaining of dysphasia is somehow more stimulating and interest-provoking than a puzzling lack of any overt pathology in a patient, who, perhaps all too loquaciously, tells a story of a dropping in the back of the throat. By virtue of his whole course of training and teaching the medical student tends to be lured by the unusual and picturesque in medicine. An "interesting case" has a universal appeal to a physician. The modern textbooks of otolaryngology are more apt to be concerned with the classical aspects of organic pathology than with these less consequential but far more common problems for a solution to which the physician may often search in vain.

For certain specialists within the specialty, whose reputation and skill have attracted to them smaller groups of patients with clean cut organic conditions, these homespun problems will occupy only a minor position in their practice but for the average laryngologist, they will make up at least a third of his clientele and happily or otherwise he must deal with them to the best of his ability if he is to satisfy the patient as well as his own conscience.

The laryngologist is perhaps more exposed to patients with homespun complaints than most other specialists. A visit to him, from the patient's standpoint is a simple procedure, free from time-consuming dressing and undressing, accessory examinations of the blood and urine, or electrocardiograms and x-rays. He anticipates that it will be only necessary for the doctor to look in his nose or throat, paint the latter or spray the former, and that after securing a prescription for some home medication, he can be happily on his way to a symphony concert or the matinee. Would that it were equally as simple for the physician.

To say that these complaints are unaccompanied by visible organic lesions, presupposes that any reasonable examination is negative or that the findings are normal. But just what constitutes a normal or negative examination? Lederer, in his inimitable way, has said that a conclusion of negative findings may be a confession of inadequate examination or improper interpretation and suggests that physicians who are bored by a complaint of nasal stuffiness or a tickling in the throat had better get a rubber stamp, if not requiring too much physical effort. Certainly the examination should be adequately thorough and painstaking, but such are the possible tests, diagnostic procedures, and laboratory measures available today that it is not easy matter to decide just what comprises an adequate examination. Common sense must enter into the picture and thoroughness should not run such riot that a sheaf of laboratory reports yields only the comforting but inconclusive information that "everything is negative."

It is a rare patient, indeed, whatever his complaint, who does not exhibit some deviation from a hypothetically normal nose or throat. So varied are the structure and physiology of the nose and throat both in patients with symptoms and those who have no complaints whatsoever, that the estimate of what constitutes normality is not always easy. Numerical measurement so valuable in examination of the blood, the urine, blood pressure, blood chemistry, and many other physiological processes in the human body is only to a very limited degree applicable to the nose and throat. Who is to assess the normal capacity of a nasal passage, the normal viscosity of nasal mucus, or the normal amount of lymphoid tissue on the posterior pharyngeal wall of any given individual? One has only to take part in a survey of hundreds of essentially healthy individuals who volunteer for such examination, to see the greatest variations in rhinological and laryngological structure and function without a hint of abnormal local sensations. When one can examine a hard-working professor's nose and observe a practically total occlusion of one nostril by a septal deviation, only to receive an emphatic denial of any difficulty in breathing, it becomes somewhat puzzling to know where normality ends and abnormality begins. Patients with enormously hypertrophied and cryptic tonsils deny ever having had a sore throat and x-rays of the nasal sinuses may reveal thickening or even polyposis of the antral mucosa in patients who scarcely ever have a head cold.

Patients voicing any one of these homespun complaints frequently exhibit a wide variety of physical deviation from an acceptably normal base. The question then arises as to whether one or more of these deviations may lie at the bottom of his complaint and hence demand correction by medical or surgical therapy. This is no easy question to settle. Is or is not that scratchy sensation or feeling of a lump in the throat due to a hyperplasia or hyperemia of lymphoid follicles on the pharyngeal wall? Is a moderate hypertrophy of the inferior turbinate the real cause of a sensation of restricted breathing? Is diminished translucency of the maxillary sinus a wholly incidental finding or is it related to a postnasal discharge?

Not a day in the office passes but the physician is forced to wonder whether these intangible and largely subjective symptoms fit, like a cross-word puzzle, with these varied physical deviations which in themselves might either escape any but the most careful examination or, in the absence of any complaints, be regarded as completely fortuitous and insignificant.

These homespun symptoms may be said to constitute a kind of sand in the laryngologist's shoes, in that they face him with a somewhat annoying perplexity in dealing with them with the same sense of assurance and confident knowledge of their nature and of how to deal with them as is the case with more visibly organic lesions. However, unfortunately for the patient, the discovery of a malignant lesion on a vocal cord or of a bleeding mass in the nose gives the physician a sense of clinical security as to his knowledge of why the patient is hoarse or why he is bleeding. Let the story be merely that of a burning feeling in the tongue or of a tight sensation in the back of the nose and one is faced at once with a diagnostic dilemma, the unraveling of which may lead into a confusing labyrinth of diagnostic possibilities. Let a patient complain of having swallowed a fishbone which is visible on a mirror examination and all is well; if no bone is seen, numerous other possibilities for the patient's discomfort must be then given consideration.

Negative findings are never quite as satisfying as positive ones, and, however much they may reassure the patient, he still seeks an explanation for his complaint. Recoveries from vague, unclassifiable symptoms with or with out treatment, logical or otherwise, are grati-

fying to the patient but are of little help in evaluating the same symptoms in a subsequent case. The satisfaction of knowing what is wrong with a patient would seem to have reached its zenith when Oliver Wendell Holmes once said that a doctor derives more pleasure in a post-mortem examination which shows what is wrong with a patient than in a case which insists on getting well and leaving him in the dark as to the cause. This, I think, is a bit exaggerated, and I assume that Dr. Holmes was not referring to a fatality following any rhinological surgery from which the patient's recovery would be preferable to any tardy revelation as to what went wrong.

Homespun laryngology, moreover, does not lend itself to research or controlled investigation. The symptoms are too intangible and varied to permit correlation with different experimental set-ups. Observations of end results is thwarted by spontaneous and illogical recovery, preventing statistical reports and comparisons of such different therapeutic modalities as surgery and radiation. The difficulty of collecting a series of cases of scratchy throats sufficient to permit any dependable comparison of two or more methods of treatment is only too obvious.

As a rule these homespun maladies do not seriously incapacitate a patient, but he is vastly annoyed by them and worried as to the possibilities which their presence may indicate, an apprehension in which he may now and again be thoroughly justified. Only recently a colleague related to me the case of a patient who came to him because of a modest sense of discomfort in the side of the neck. A most comprehensive examination was carried out without revelation of the cause. The patient's persistent complaints led finally to a surgical exploration and discovery of a carcinoma of the thyroid gland. The first sign of leukemia may be a simple epistaxis. The local symptoms here being discussed may, when least expected, lead to the discovery of hormonal imbalance, metabolic disorders, dietary indiscretions, faulty habits of living, of sleep, exercise, and work. It is the ever present possibility in each individual, rare as it may be, of a serious condition that makes it imperative to give due credence to the patient's complaints and carry out adequate investigative measures before assuming the absence of any organic disease.

Today, with the extensive propaganda being broadcast concerning the early detection of cancer, many patients, while not expressing

overt apprehension, are secretly worried lest the sense of irritation in their throat may portend the early development of a malignant growth. They seek, quite apart from relief of their discomfort, what Sir Herbert Tilley so happily referred to as the "solace of an optimistic report." Even when, as in the great majority of cases, such reassurance can honestly be given, the patient still wishes to know the cause of his symptoms and to be afforded the means by which he may be rid of them. It is in this respect that these homespun complaints tax the acumen and judgment of the physician quite as much as if they were due to a more serious but readily observable lesion.

One of the major difficulties in establishing a diagnosis in this group of symptoms here under consideration is a multiplicity of etiological possibilities underlying a specific complaint. A simple cough may be associated with turbinal hypertrophy, an elongated uvula, a granular pharyngitis, a lingual tonsilitis, or an irritated larynx. Let us look for a moment at that protean bane of the rhinologist, postnasal discharge. Described by Proetz as "the great American nightmare" (whether for the patient or the physician he does not specify), this common complaint is ascribed to some fifteen widely diverse etological possibilities, each indicative of such differing therapy as to leave one quite bewildered as to which avenue of treatment to pursue. It is not hard to appreciate the diagnostic dilemma of the rhinologist who is confronted on a cold New England afternoon by a woman in the menopause, unhappily married, and inordinately fond of chotoclates, who is seeking relief for a dropping in the back of the throat. Her examination may reveal a slight hypertrophy of the inferior turbinates, some enlargement of the lymphoid follicles on the posterior wall of the pharynx, or a moderate deviation of the septum. Is one to apply carbolic acid to the turbinal tips, are the lymphoid nodules to be painted with silver nitrate or is she to be afforded questionable help from a submucous resection? If, however, the local examination offers no possible therapeutic objective, is she to be told to put pans of water on the radiators, to take hormonal injections, to leave her husband, and for good measure move to Arizona, or just to give up candy? This hypothetical situation may seem unduly exaggerated but any one of these suggestions in a given case may yield such happy results that some consideration of all of them must enter into the solution of the problem. Atmospheric changes, exposure to external irritants, emotional tensions, endocrine

and metabolic disturbances, plus a wide variety of local nasal abnormalities—all may in a given case justifiably claim attention. The far simpler causal relationship between hoarseness and laryngeal tuberculosis makes for infinitely easier decision than in the case of postnasal discharge.

A physician's personal hobbies go far in determining what he regards as an adequate investigation into the causes of a particular symptom. Thus to an allergically minded rhinologist postnasal discharge might warrant the subjection of the patient to a battery of skin tests and a seance with a questionnaire of some 300 queries. The enthusiast for dietary modifications as the sovereign remedy for this widespread complaint proceeds on a totally different line of attack, often quite as successfully as the allergist. The endocrinologist feels sure that corticosteroids will solve the problem. The cost to the patient in time and money of such excursions into allied medical fields is not hard to visualized, but each physician can cite cases to justify his personal enthusiasm for a given line of approach. In addition it must never be forgotten that the origin of a patient's complaints may lie in some area remote from its apparent location and so bring into question a general physical examination of his blood, urine, chest, heart, or gastro-intestinal tract, or other areas not visualized with a head mirror.

The problem of multiple etiology, within limits, holds good for many of these homespun complaints, the investigation of which, in modern medical practice and with the availability of numerous and seemingly unrelated procedures may lead one far afield. It is no easy matter to steer a reasonable course between thoroughness and overly exhaustive coverage of every possible diagnostic measure.

Such patients often present themselves at the end of a busy day when the physician is hard put to it to give the time and attention to what may seem like a tedious and indeed loquacious recitation of complaints which he cannot but feel are somewhat inconsequential and yet to which he must give sympathy and patience if he is to get at the root of the matter. He may well wonder after reading perhaps of the terrifying experiences of survivors on the Andrea Doria, how patients can place so much emphasis on such seemingly minor discomforts, but philosophers long ago maintained that sym-

pathy for the misfortunes of others does in the least mitigate the poignancy of our own. These patients with rare exceptions are genuinely troubled by their ailments, do not complain simply to irritate the doctor and expect some return for their time and money beyond the pleasure of being coddled and fussed over. It takes time to hear these stories, more time than can usually be given by a man who sees 30 or 40 patients in a day. Often the physician earns his money by the dose of loquacity he takes himself quite as honestly as the pharmaceutical one which he prescribes.

If, by whatever measures he deems advisable for purposes of adequate examination, both locally and systemically, the physician can satisfy himself that there is no demonstrable organic cause for the patient's complaint, he may then justifiably conclude that the case falls into the ever-increasing and more frequently recognized category of psychosomatic. Since the earliest days of medicine it has been known that pathological states may often be the reflection of some emotional or nervous tension quite as definite as of actual organic disease. Symptoms of gastric ulcer, of sinusitis, even of a brain tumor may stem from some social, economic or moral conflict of which the patient himself may be only vaguely aware, but which may closely simulate organic disease. Functional disorders, with which the symptoms here under consideration are frequently associated, are today occupying an ever-increasing portion of otolaryngological practice. Modern life is, as never before in history, being lived for countless individuals under the strain of world unrest, the threat of war, economic confusion, and a hypertensiveness of daily activities that subjects even the most well adjusted person to a degree of tension, consciously or unconsciously, which may express itself in local symptomatology in so sympathetic an area as the nose or throat. Davison has estimated that 36 per cent of a large group of office patients manifested only functional disorders while 22 per cent more had a combined functional and organic origin, a total of 58 per cent of all patients presenting some functional elements in their complaint. It thus devolves on the laryngologist to take a far wider view of his patient than what can be seen in the nose or throat. This is not to say that he must, in addition to his special field, assume the role of the psychiatrist, for which he has neither the time nor the training. If, however, he is willing to give attention and consideration to the patient as an individual, to assess his general appearance, personality

and manner of presenting his complaint, he will be surprised with what ease he can frequently come to a quite dependable and justifiable conclusion that his patient's trouble stems from some underlying emotional tension of which the symptoms are unlikely to be attributable to anything seen on local examination. Because these seem to neurotic on whom no further time need to be expended. Patients are universally resentful of a physicians' attitude which suggests that they are hypersensitive, that they are complaining unjustifiably or lack classification as a clinical entity is no proof that the patient is a that they merely imagine the existence of their trouble.

TREATMENT

If the establishment of a specific cause of these assorted symptoms is difficult, the decision as to how they are to be treated is no less so. The removal of a questionably infected tonsil, the correction of a moderate septal deviation, the excision of a slight turbinal hypertrophy may occasionally achieve gratifying results but more often will prove unavailing in eliminating the patient's complaint. Most patients do not relish surgical procedures unless given convincing assurance of a direct causal relationship between their symptoms and the objective of the surgery and it is far from satisfying to the surgeon to observe a pleasing operative result in a patient who still presents his original complaint.

Throughout all otolaryngological literature there runs periodically the outcry against unnecessary surgery, as witness in 1926 Shambaugh's criticism of indiscriminate tonsillectomy as the "most flagrant abuse in the practice of medicine." His contention that "most patients with headaches do not have sinusitis and most patients with sinusitis do not have headaches" is, I think, as true today as 25 years ago. It is particularly in conjunction with the type of complaint here under consideration that operative procedures should be withheld unless a successful result is virtually assured.

The advisability of less drastic therapeutic measures may present equally perplexing decisions. Local applications, sprays, cauterizations and packs offer tempting opportunities to do something tangible for the patient, and when least expected may afford prompt and

gratifying relief, but inevitably leave the physician with a feeling that good luck rather than logical management has turned the trick. There is always the risk that such treatments, particularly if repetitious, will lead to some degree of fixation of the patient's complaint who thereat assumes that he must have some visible disorder for which he would not otherwise be given treatment. At the other end of the scale lies therapeutic nihilism, with the withholding of any treatment which cannot be logically justified, leaving the patient to utter that classic complaint, "he didn't do anything for me." These are not easy decisions to make for a conscientious doctor who is still eager to help his patient.

One of the currently popular television and radio advertisements extolls the merits of a certain drug because it is, to quote, "like a doctor's prescription." Many a patient, however reassured by his physician of an absence of any serious findings, will be disappointed if not given a prescription. It is a common observation at the American Academy Instructional Courses that the instructor who is equipped with prescriptional novelties will have every seat in the room taken. If at the conclusion of his examination the laryngologist is uncertain as to the exact nature of the patient's ailment, he will be tempted to hope that a trial of some prescription will at least satisfy the patient or perhaps even cure him. Never before has there been such a multiplicity of therapeutic possibilities for every known ailment or symptom as is today flooding the market. The morning's mail brings an armful of gaily colored and sample-bearing panaceas allegedly appropriate for numerous disorders or complaints. Toward these it is impossible to maintain a scientifically critical attitude based on controlled experimentation. Such hit-or-miss therapy will seldom leave the physician with any very satisfied feeling of professional achievement, regardless of the patient's frequent report that the medicine has done him a world of good.

Moreover, the results with any given drug or procedure will always vary because inevitably applied under slightly different conditions and to different individuals and what is proclaimed by one physician as a sovereign remedy or mode of procedure may often disappoint an equally competent colleague.

The rise in frequency of emotionally based complaints goes hand in hand with an increase in the number of so-called tranquilizing

drugs for which over 35,000,000 prescriptions were written in 1956, among them an unknown number for one drug advertised as efficacious in 17 different conditions ranging from mental deficiency to arthritis. It has been estimated that in ten years the pharmaceutical industry will be one of the top ten in the country. For the moment, drug houses seem overly concerned with Relaxors, Tensors, Neutralizers, and Antagonizers, creating an impression that today there is available a drug for every mood, every stress, and every strain to which mankind may be subjected.

The question arises as to how far the laryngologist should attempt the role of psychiatrist. Certainly he is not to be expected to undertake a lengthy and specialized psychiatric investigation, but if he is willing and sufficiently interested to give the time, patiently and sympathetically, to talk to the patient he will be surprised to find how often even a superficial inquiry into a possible emotional cause of the symptoms will bring to light something of which the patient is quite ready, even eager, to talk if given only a helpful suggestion and encouragement. At the outset patients with laryngological complaints are quite unprepared to find a laryngologist interested in their personal problems and are equally unaware that there may be any connection between these and their local symptoms. Once the laryngologist has overcome a natural reluctance to investigate the less familiar emotional background, he will discover how readily a comfortable relationship can be established and how frankly the patient will reveal a possible underlying explanation for his symptoms. A woman who leaves the office in tears has often been more effectively helped toward riddance of a stuffy nose than one whose turbinate has been cauterized or who has been given an antihistamine or a tranquilizer.

It is with some reluctance that I bring to the attention of so distinguished a group of laryngologists a subject unrelated to experimental research, novelties of technique or statistical surveys. My interest in this subject is the outcome of prolonged soul searching as to how these daily problems should best be handled from the patient's standpoint. Quite possibly I shall have benefited more than my audience from what is to some extent a personal confessional. In this homespun segment of our work, however lacking in glamor, there is always opportunity for the industrious, a challenge to solve prob-

lems, and the gratification of achieving good results of which a patient will often be quite as appreciative as of those attained by more spectacular procedures.

The sand in our traveler's shoes may have been annoying but, through toughening his feet, it may have facilitated his conquering the more formidable hazards of his journey. The daily training in dealing with the homespun complaints I have considered may well prove of unsuspected value in improving our handling of the more dramatic and colorful problems in laryngology.

77 Massachusetts Ave.

LXIII

FUNDAMENTAL PHYSIOLOGICAL FACTORS TO BE CONSIDERED IN SPEECH THERAPY

W. W. Wilkerson, Jr., M.D.

AND

Forrest M. Hull, Ph.D. (by invitation)

Nashville, Tenn.

The production of human speech requires the functional integration and synchronization of several physiological systems. Although there is an area of agreement in regard to the physiology of speech, many facets of this activity are unknown.

The basic requirements for voice production include the breathing mechanism, the larynx, and resonators. In the consideration of speech production it is necessary to add a fourth physiological system, the articulators.

Included in the articulators are the tongue, pharynx, palate, lips, and the teeth which are also integral components of the speech resonating system. Each of these speech physiological systems and structures functions primarily and initially to sustain life. For example, the sphincter action of the larynx protects the lower respiratory tract, and by partially controlling intrathoracic and intra-abdominal pressure the larynx exerts some control over blood circulation, blood pressure and the interchange of gases in the lung. In the production of speech it is necessary to modify these primary functions in order to produce acoustic signals, which in a sense interferes with the original purpose of these systems. For this reason speech is referred to as a secondary function, primarily controlled by the central nervous system.

From the Bill Wilkerson Hearing and Speech Center, and the Department of Otolaryngology, Vanderbilt University School of Medicine.

The physiological activity of all of the component parts utilized to produce speech may be influenced by:

1. Mental retardation.

2. Organic brain damage, cortical or subcortical. This is a rare condition which frequently has been incorrectly diagnosed.

3. Abnormality of anatomical structures.

4. Lesions of the V, VII, VIII, IX, X, and XII cranial, the intercostal, spinal and phrenic nerves and the sympathetic plexus.

5. Lesions in different areas of the central nervous system producing various muscular abnormalities such as loss of co-ordination, involuntary movements, spasms, and weakness.

6. Increased or decreased activity of the salivary glands and the glands of the upper respiratory tract.

7. Diseases such as myasthenia gravis and Friedreich's disease.

Oral communication in its simplest form is cyclic in nature involving the mechanics of speech and hearing. If the hearing of the speaker is impaired his speech monitoring system is disturbed. An "acoustic memory" is also a prerequisite for normal speech. The role of hearing in speech production is of major importance and must be included in any consideration of speech behavior.

In the field of speech pathology and speech therapy, voice and articulation disorders, although related, are routinely considered separately, and as different problems. There are observable differences in that each has its individual characteristics requiring special considerations.

The fact that the same physiological system can be used to produce acoustic signals perceived as speech which differ enough to prompt their description in different terms indicates clearly the high order of physiological integration which exists for speech. It also strongly suggests that the same fundamental principles can apply to both voice and articulation disorders.

There are two aspects of physiological function: first, limitating factors (normal and abnormal functioning) and second, compensatory functions.

FUNDAMENTAL PHYSIOLOGICAL PRINCIPLES INVOLVED IN CONSIDERATION OF SPEECH THERAPY

In a speech disorder, the physiological systems have not been integrated functionally to produce acceptable speech. Any voice or articulation speech disorder can be fitted into this frame of reference.

All cases with abnormal speech deserve an otolaryngological examination, and perhaps other medical and dental examinations prior to speech therapy. Dentistry has an important role in the speech field.

Pitch in the human voice is directly related to the rate of the vocal fold vibration while quality is related to the manner in which the vocal folds vibrate. However, quality is even more closely related to the influence of the resonating cavities. Even so it has been demonstrated that voice quality can be changed by merely elevating the pitch.

Application of this principle is illustrated by the following case report:

REPORT OF CASES

A 48 year old male complained of tightness, distressing fatigue, and pain in the throat after talking for only a short time. The quality of the voice was obviously deviated from the normal. The tones appeared to rattle as if something loose on the cords was interfering with their movement. The pitch did not sound abnormally low. A laryngeal examination was negative. In the speech analysis the pitch range was calculated to be approximately 13 musical notes, which was abnormally restricted. Further, it was found that the patient habitually spoke quite near the lower end of his pitch range.

Voice training was employed to increase the pitch range and especially to raise the habitual pitch level. Eventually the patient developed a pleasing and normally effortless voice pattern.

The significant point which is illustrated by this case study is the fact that elevation of the fundamental pitch resulted in altering the quality of the voice.

Laase[1] in 1937 demonstrated that, under controlled conditions, the quality of the human voice is altered perceptibly by simply elevating the fundamental pitch. This indicates a physiological relationship between the vocal fold activity which is responsible for the fundamental pitch and the resonators which are the primary determinants of voice quality.

The following case report indicates the necessity of a laryngeal examination in all cases with a speech abnormality.

A young adult male manifested a voice disorder which was diagnosed medically and by the speech pathologist as severe harshness. Vocal nodes were present bilaterally, otherwise the laryngeal examination was negative. The nodes were removed, but the harsh quality persisted except in one pitch, despite voice therapy. Direct laryngoscopy showed the presence of some scar tissue on the cords which may have interfered with their normal synchronous vibration. The harsh quality still remains after a period of over three years following surgery and voice therapy.

In order to understand this problem one must analyze the fundamental function which is responsible for the deviated voice quality. It is a well established fact that in a normal voice the manner of vibration of the two vocal cords is synchronous and in a complex wavelike motion. The tone thus produced is periodic and complex with a predominant musical or clear quality. This, of course, is due to the inherent characteristics of the vocal folds. The cords are elastic and can be stretched, which changes both the length and stiffness. When this occurs the pitch is elevated but the quality of the tone is not distorted which implies that the synchronous vibration pattern has not been altered. There are numerous causes of harsh quality but in regard to the disorder of the case just reviewed it seemed possible that the amount of scar tissue remaining on the vocal folds was sufficient to preclude a normal pattern of fold vibration. Although the human organism can compensate for some deviations of structure and function, there is a limit which cannot be exceeded.

This limit lies within the anatomical and functional characteristics of the structures involved. Knowledge of these factors makes it possible for the voice therapist to approach individual voice problems realistically.

A significant case, B.B., age 16, white female, whose family and previous history were negative, had acute spinobulbar poliomyelitis in January 1954. Three days after the acute onset she developed facial paralysis, inability to protrude her tongue and to swallow. A tracheotomy was required, followed by almost constant suction. Two days later, paralysis of the abdominal, respiratory muscles and of all of the extremities was noted. She was placed in an Emerson respirator and five days later the acute symptoms began to subside. At this time the patient was speechless.

When first seen, two and a half years later, the findings of her physical examination were not remarkable except for neuromuscular changes.

The patient had bilateral paresis or paralysis of the V, VII, X, XI, and XII cranial, and the intercostal, spinal and perhaps the phrenic nerves.

At the present time the paralysis of the V cranial nerves involves the masseters, temporals, pterygoids, myelohyoids and anterior half of the digastric muscles. Contracture of these muscles with some fibrosis of the joints' capsules had resulted in the inability of the patient to open her mouth more than one-half inch. The paralysis was responsible for the patient's inability to close her mouth.

Physical therapy has made it possible to open her mouth so that a prothesis can be applied which enables her to approximate her mandible without the use of a Thomas collar.

The platysma, the buccinators, the posterior half of the digastrics, the stylohyoids, the epicrani, and the other superficial muscles of the face show evidence of involvement of the VII cranial nerves. That involvement is minor and produces little speech difficulty. There is a loss of function of the levator palati, constrictors of the pharynx, and the intrinsic muscles of the larynx due to involvement of the X

and XI cranial nerves. Almost complete paralysis of the XII cranial nerves has produced paralysis and atrophy of the intrinsic muscles of the tongue. The tongue tends to drop back into the pharynx and the patient is incapable of protruding it.

Therefore the patient's speech difficulty arises from:

1. Paralysis of the muscles of mastication which prevent her from moving her mandible.

2. Contracture of the same muscles which have left the mandible in a closed, fixed position with a marked underbite.

3. Paralysis or paresis of the muscles of the pharynx and larynx.

4. Marked paralysis and atrophy of the intrinsic muscles of the tongue.

Gradually speech returned until at the present time it is intelligible and in connected form. Most patients who survive poliomyelitis do not manifest significant articulation disorders. Examination reveals that the patient is not articulating the speech sounds in a normal manner, as it is impossible for her to use the usual speech structures.

The results of the analysis of the articulatory movements of this patient show that she has been able to relearn almost acceptable articulatory patterns by means of, what should be termed, very ingenious compensatory movements. These compensatory movements consist principally of utilizing a combination of lower lip and upper teeth contacts for the production of consonants which are normally articulated by the tongue in contact with the internal oral structures and the teeth. The glottis is substituted for the tongue to produce plosive sounds "k" and "g." She has learned all these compensatory movements without instruction.

The "k" sound in the word "cat" is a stop-plosive consonant normally produced by elevating the back of the tongue to contact the velum during which time air pressure is increased. The tongue is then dropped suddenly and the plosive phase of the sound is completed. This sound is voiceless and therefore the vocal cords do not

vibrate at any time. In the compensatory "k" sound the glottis is closed with an increase in subglottal air pressure. At the plosive stage the glottis is opened suddenly and the resultant sound cannot be differentiated from the normal "k" sound.

This in itself is not unique as it occurs not infrequently in speech disorders. Similarly, the compensatory "g" sound is produced with the glottis. Normally, the only differentiating characteristic between "g" and "k" is that the "g" is voiced (vocal folds vibrate) and "k" is voiceless (vocal folds not vibrating). It is significant that compensatory speech movements could be so discretely adjusted as to result in such minute differences confined to the same anatomical structures.

This case study clearly illustrates the ability of anatomical structures to assume unfamiliar functional activities, in a logical and optimal manner. For example, the glottis is easily adapted to produce glottal clicks as required for explosive bursts of air. The other structures involved could be analyzed in a similar manner.

The results of this case study also imply a more flexible approach to speech therapy. Usually the speech therapist attempts to retrain or train the speech structures to function as they should normally. However, there are many disorders, such as cleft palate and cerebral palsy, wherein the damage to the speech mechanism structure is so extensive that normal functioning is impossible. With such cases compensatory speech could possibly result in a more acceptable speech pattern if judged only on the basis of the acoustic impression.

SUMMARY

Fundamental integrated factors should be considered in any speech therapy approach as they determine the extent of the changes in speech through therapy. The examples cited suggest three fundamental principles which should be used as basic speech therapy rationale:

1. It is important to understand the nature of individual mental physiological activities and their integrated interrelationships.

2. Direct damage to speech producing structures may be extensive enough to preclude training or retraining of these areas in order to produce acceptable speech.

3. It has been shown that compensatory movements can be developed. Therefore one should explore the possibilities for introducing compensatory activity for speech rehabilitation whenever there exists extensive organic damage of the speech structures.

In the case of the patient with poliomyelitis, vocal fold activity was successfully substituted for movements which are normally the responsibility of the tongue.

700 Church Street

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LXIV

THE MECHANISM OF PHONATION

Sir Victor Negus

With the Collaboration of

Professor E. Neil and Dr. W. F. Floyd

London, England

For many years I have taken great interest in the study of the anatomy and physiology of the larynx; I have found it essential to examine all the functions of the organ and the conclusion, based mainly on the evidence of comparative anatomy, has been that in mammals and man an organ evolved and developed for other purposes has been adopted for producing cries, speech and song.

The larynx is not utilized for this purpose by all species, as for instance birds, who have evolved a specialized vocal organ, the syrinx; no doubt mammals could have done the same if the necessity had arisen.

One commences, therefore, with the assumption that the physiological principles entailed in such processes as protection of the respiratory tract or fixation of the thorax during fore limb efforts, are similarly used for the production of sound. It would be surprising and to me impossible to believe that entirely new physiological principles had been introduced for phonation in an organ not primarily designed for that purpose.

Furthermore I am a firm believer in the lessons of comparative anatomy; I do not accept any suggestion that the human body has evolved mechanisms differing basically from those of other mammals.

Examination of minute structure shows a remarkable similarity between the individual components of the animal and human body;

From the Department of Physiology, Middlesex Hospital Medical School, London.

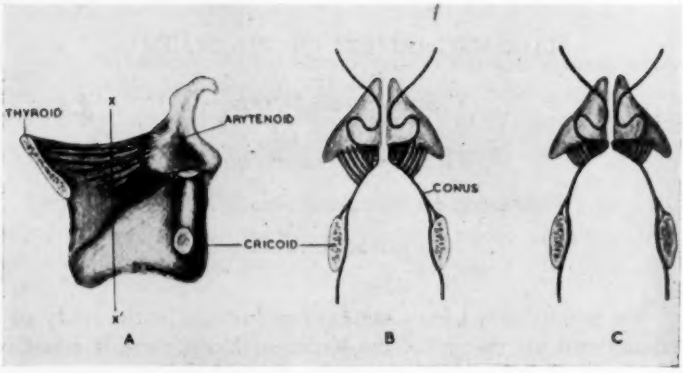

Fig. 1.—Diagram to represent registers. In B is seen a coronal section of the larynx of a man during the production of low pitches; deep areas of the inferior thyro-arytenoid folds come into contact. In C is represented the mechanism for high pitches; contraction of those fibres of the thyro-arytenoid muscle arising from the conus elasticus has reduced the areas meeting on phonation. On the left (A) the shorter course of the fibres arising from the conus is shown in relation to those coming from the thyroid cartilage.

to take one example, cilia have been shown to correspond in structure, whether taken from a mollusc, an amphibian or a mammal.

Having read many communications on the subject of phonation and having examined the larynx of most vertebrates, including man, both anatomically and experimentally, an understanding of the mechanism had been attained which seemed to offer a clear and logical explanation.

But having arrived at this degree of comprehension, philosophical doubt has now been cast by the introduction of a new clonic theory of phonation as an alternative to that previously held. It is obviously desirable to examine this theory and not to ignore it because of its divergence from previously recognized opinion.

The reason for the introduction of these new and original views depends on the difficulty experienced by their authors in explaining certain details of phonation on orthodox lines; three or four supposed

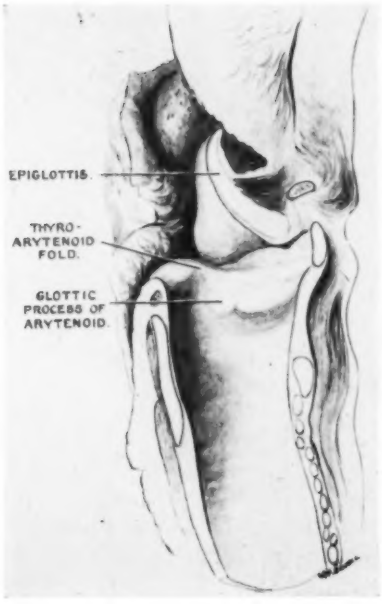

Fig. 2A.—Sagittal section of the larynx of a spotted hyaena, Hyaena crocuta, to illustrate the absence of a separate inferior thyro-arytenoid fold. With a similar simple type of larynx many members of the cat tribe execute a wide range of sounds.

discrepancies have led to the discarding of the old and the introduction of a new explanation.

I do not propose to deal with these details, which to me do not offer valid objections to the views previously held. Rather is it desirable to examine the basic principles underlying the alternative theories; if one or other is proved correct or if either is found to be untenable then it will be time to pay attention to the details in dispute.

BASIC PRINCIPLES OF PHONATION IN MAMMALS

The sound producing system consists of three parts, bellows, reed and resonator; there is no dispute as to these elementary details. The

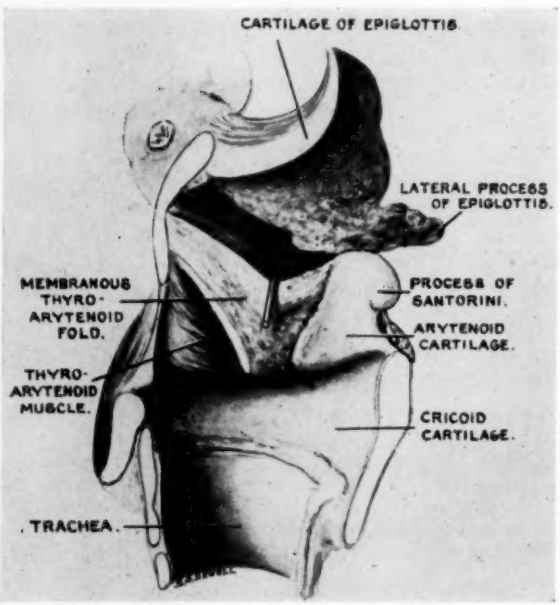

Fig. 2B.—Dissection of the larynx of a spotted hyena. The lax connective tissue covering the thyro-arytenoid muscle is shown, unlike the vocal fold and conus elasticus of man. The thyro-arytenoid muscle is flat and its fibres arise from the thyroid cartilage, to be inserted into the arytenoid; there is no origin from the conus and no possibility of separation of the margins of the glottis by muscular traction except by the action of the posterior crico-arytenoid muscle.

bellows are provided by the lungs; with a stream of air under varying degrees of pressure audible laryngeal sounds cannot be produced. Again, there seems to be no dispute regarding the dependence of loudness or intensity on the pressure of the air stream escaping through the larynx.

There are, naturally, differences in the pressure required to actuate various types of larynx; for instance, the small Hoolock gibbon can produce piercing cries of amazing loudness by virtue of the nature of the vibrating folds at the glottis.

There is, I believe, no disagreement in regarding the larynx as the source of sound in mammals; mixed sounds are produced at the glottis under the agency of the actuating tracheal air current.

The third component comprises the resonators of the thorax, the pharynx, the mouth and nasal passages; by their agency the quality of sound is mainly controlled, together with amplification of the mixed laryngeal tones; by themselves the latter are feeble and of poor quality, as noticed when a subject of laryngectomy attempts to phonate after his larynx has been separated from the pharynx, while still attached to the trachea.

If I am right in assuming that both tonic and clonic theories ascribe control of loudness to the lungs and determination of quality to the resonators, then the argument resolves itself into differences of opinion regarding sound production at the glottis.

TONIC AND CLONIC THEORIES

The usual explanation of phonation ascribes the production of laryngeal sounds to rhythmical opening and closure of the glottis under the influence of intratracheal pressure. The mechanism does not resemble any known musical reed, because it depends on varying elasticity of the glottic margins, as determined by the degree of contraction of the muscles bounding the glottis. These are the thyro-arytenoids, which contract slightly or powerfully to support the overlying connective tissue or vocal folds, which come into apposition with one another, with temporary closure of the glottis; the pressure of air in the trachea then blows the closed folds apart and the consequent reduction of pressure allows their elasticity to close them once again, the process repeating itself rhythmically.

Here the active agent is intratracheal pressure, which causes a series of puffs to escape through the tonically closed glottis. Experiments with strips of muscle or with an excised larynx readily demonstrate this mechanism.

The clonic theory, on the other hand, is based on rhythmical contraction and relaxation of the muscles bounding the glottis, that is the thyro-arytenoids, under the stimulus of a succession of nervous

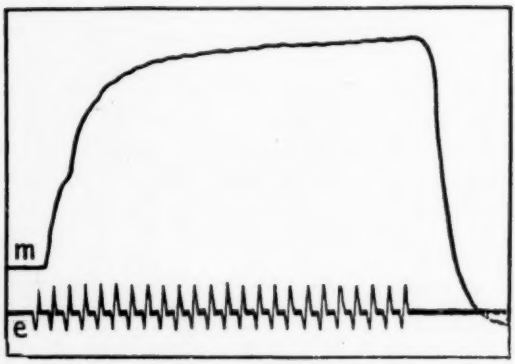

Fig. 3.—Mechanical (upper record) and electrical (lower record) responses of muscle to stimulation of its motor nerve at a rate of 67 shocks per second. Note fusion of mechanical contraction although discrete e.m.g. potentials are still seen. (Sherrington et al. Reflex Activity 1932) (Reproduced from Applied Physiology. Samson Wright. H. Milford. Oxford University Press.)

impulses derived from the central nervous system; here the active agents are the margins of the glottis, with release of intratracheal air in a series of puffs.

ROLE OF OPPOSING MUSCLES

In both tonic and clonic theories it is understood that the muscles bounding the vocal folds, the thyro-arytenoids, are afforded fixed points of origin from the thyroid cartilage, with insertion into the arytenoids. Consequently, it is essential that the thyroid and cricoid cartilages should be held in correct relative position by the cricothyroid muscles, that the arytenoid cartilages should be braced back against the pull of the thyro-arytenoids by contraction of the crico-arytenoideus posticus, and that the arytenoids should be held in firm apposition by the interarytenoid, the lateral crico-arytenoid and partly by the external division of the thyro-arytenoid muscle.

If this assumption is accepted the argument confines itself to a study of the thyro-arytenoid to decide whether its components are in tonic or in clonic contraction.

ACTION OF OBLIQUE FIBRES OF THE THYRO-ARYTENOID MUSCLE

The exponents of the clonic theory have introduced a further complication. Instead of supposing that the thyro-arytenoid alternately contracts and relaxes, thus releasing puffs of air, they have suggested that oblique fibres of the thyro-arytenoid muscle, or transverse fibres according to their writings, pull the glottic margins apart rhythmically.

Dissections of the human larynx show that there are oblique fibres of the external division of the thyro-arytenoid, arising from the outer surface of the conus elasticus, to be inserted into the body of the arytenoid. The origin is, however, low down and not from the upper part of the conus which constitutes the fibrous covering of the vocal fold; contraction would not open the glottis but would only pull the subglottic membrane outwards (Fig. 1).

The presence of oblique fibres is well recognized; the action usually ascribed to them is the production of what are known as thick and thin registers. On low tones, when elasticity of the glottic margins is at a minimum, with contraction of only a few muscle fibres, the conus is not pulled outwards and a broad surface of the inferior thyro-arytenoid or vocal fold comes into contact with its fellow.

Moving pictures with a very high speed camera show the somewhat flabby, wide faced folds being blown apart from below upward, rolling outwards as the puff of air escapes.

On high tones, when many or all the fibres of the thyro-arytenoid are in contraction, those directed obliquely pull the conus outwards and thus reduce the areas of the vocal folds in contact; this is called the thin register, clearly demonstrated by tomograms.

Most mammals, including monkeys, have no such oblique muscle fibres (Figs. 2A, B); on comparative and human evidence, I consider the introduction of this complication to be unnecessary, inaccurate and unfortunate.

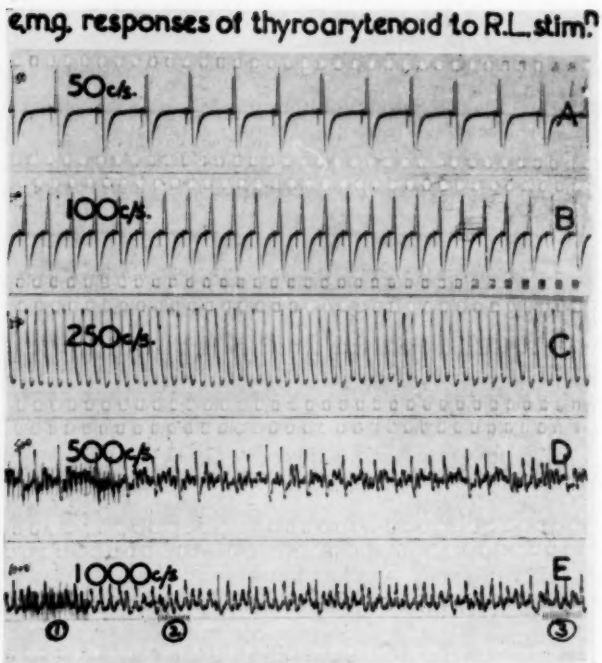

Fig. 4.—E.m.g. records from thyro-arytenoideus during stimulation of the recurrent laryngeal nerve at 50, 100, 250, 500 and 1,000 c/s. In D and E the stimulus artefact has been touched up to show more clearly. In E this has been done at three points (1), (2) and (3). Note that in E the e.m.g. potentials occur at a much slower rate than that of the stimulus artefact.

CENTRAL NERVOUS CONTROL OF PHONATION

Considerable emphasis is placed by the clonic theorists on the centers and tracts in the cerebrum, the midbrain and the hind brain; it would appear, however, that observations in this direction have no direct bearing on the problem.

The neuromuscular mechanism of phonation is remarkably complicated, since there are not only the many muscles of the larynx to

be controlled, but in addition those of the pulmonary system and also those of the various resonators; there are at least one hundred single or paired muscles.

When it is remembered that air must be expelled from the lungs at an even pressure of varying level, it is obvious that delicate control of the intercostals and diaphragm, among others, is required.

As to the resonators, the shape and size of the pharynx and mouth must be adjusted; the soft palate, the tongue, lips and cheeks all need control, with frequent changes when vowels or consonants are pronounced.

To the larynx are attached a number of muscles, the sternohyoid, thyrohyoid and sternothyroid, the palatolaryngeus and inferior constrictor; there are also the intrinsic muscles, two paired and one single.

If one considers an operatic singer it is amazing to observe the ability to produce tones in competition with a large orchestra, to alter pitch and at the same time to articulate, all with theatrical emphasis. The cerebrum has an immense task in sending out signals to the subsidiary centres, which in turn co-ordinate and relay stimuli to the many muscles. To attain purity of quality the degree of contraction of the right and left thyro-arytenoid muscles must be identical so as to afford equal elasticity and equal rapidity of recoil to the two vocal folds.

The neuromuscular mechanism of the tonic theory is thus found to be extremely complicated, and at first sight almost overpowering.

The clonic theory envisages similar control of the whole system, with tonic contraction of all the muscles except the thyro-arytenoids, which are supposed to contract rhythmically and, as in the tonic mechanism, with identical force on the two sides.

The burden on the central nervous system according to the tonic method is sufficiently onerous, but the addition of clonic contraction of two small muscles would appear to be more than could be expected.

The main point of this section of the discussion is not merely to refer to the complexity of the nervous control, but to show that

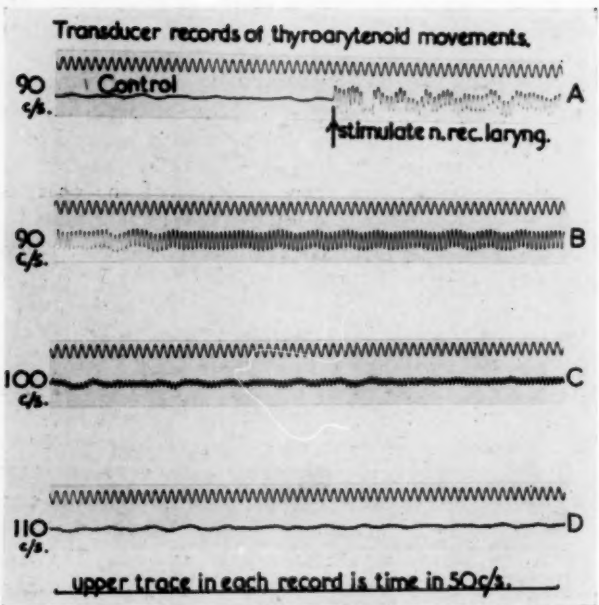

Fig. 5.—Transducer records of movements of thyro-arytenoid muscle of cat during stimulation of the recurrent laryngeal nerve at frequencies of 90, 100 and 110 c/s. Note the absence of clonic movements at 110 c/s.

consideration of the central nervous system and its pathways cannot lead to any decision as to the validity of one or other theory.

THEORETICAL OBJECTIONS TO THE CLONIC THEORY

The most rapid rate of contraction of skeletal muscle is reported by Ladd Prosser to be in the wing of a fly, which vibrates at a rate of 330 per second. Even if this were possible in the larynx, it would not affect the argument, since vocal pitches as high as 2048 C/S have been recorded.

Many years ago Sherrington demonstrated that if a skeletal muscle be stimulated by rhythmical electrical impulses, it goes into

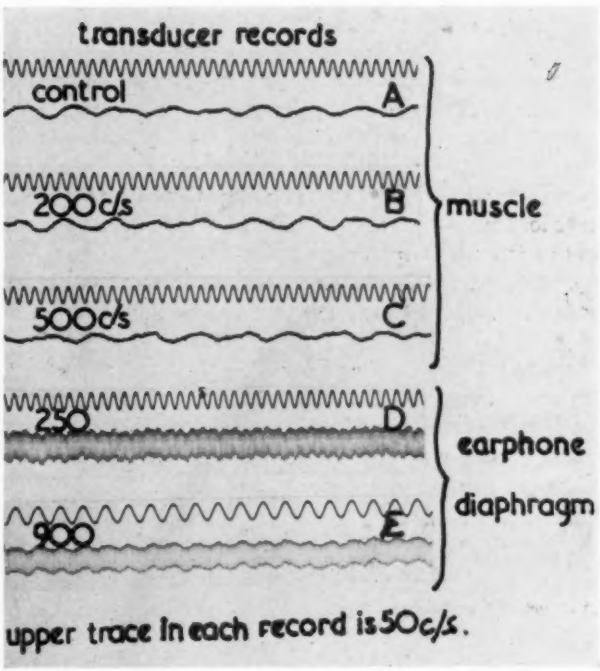

Fig. 6.—Transducer records. A, B and C were recorded from the surface of the thyro-arytenoid muscle. B and C were taken during stimulation of the recurrent laryngeal nerve at frequencies of 200 and 500 c/s respectively and show no difference from A which was recorded in a control period during which the recurrent laryngeal nerve was not stimulated. D and E were recorded by the transducer system with the transducer probe resting against the diaphragm of an earphone vibrating at 250 and 900 c/s respectively. The amplification used in the transducer recording was the same throughout. Note that the transducer responds to movements at a frequency of 900 c/s.

tonic contraction (Fig. 3). If electromyographic potentials (e.m.g.) be picked up from the contracted muscle they are found to correspond to the rate of stimulation of the muscle, which, however, does not contract clonically, but remains in tonic contraction or tetanus, even when the stimuli are no more than 67 per second.

The conclusion is that the mere recording of induced action potentials is no evidence that the muscle is in rhythmical or clonic contraction.

The main practical support for rhythmical contraction of the thyro-arytenoid muscle appears to be the recording of action potentials during phonation; there is no reason why there should not be indications of clonic contraction at slow rates, but only, as will be demonstrated later, at pitches below those of ordinary phonation in man.

Anyone who has heard the piercing high-pitched cries of a gibbon will, on this evidence alone, doubt the possibility of clonic contraction; dissection of the larynx of such an animal shows upturned, valvular inferior thyro-arytenoid or vocal folds, with no attachment of the adjacent muscle to their membranous coverings.

EXPERIMENTAL EVIDENCE

I have been fortunate in arousing the interest of Professor Neil and Dr. Floyd, whose expert knowledge of physiological problems has been of extreme value; their access to electrophysiological apparatus and their experience in its use have allowed theory to be supported by practical demonstration.

Experiments were carried out in the Middlesex Hospital Medical School on the larynx of cats, with rhythmical stimulation of the recurrent laryngeal nerve, the electromyographic response (e.m.g.) of the thyro-arytenoid muscle being recorded at the same time by means of a cathode ray oscilloscope. At frequencies of 50 and 100 C/S a large response followed each stimulus and at rates as high as 250 C/S occasional response was found in the muscle (Fig. 4).

At higher frequencies, however, there was no obvious relationship between the e.m.g. potentials and the stimulation frequency.

These experiments indicate that although the muscles bounding the glottis might contract rhythmically at low rates, yet at higher frequencies they obey the laws of other muscles and go into tetanic or tonic contraction, as envisaged in the usually held theory of phonation.

A second series of experiments was carried out by means of a piezo-electric transducer. This consists of a slender steel wire resting against the free margin of the thyro-arytenoid fold, its other end being fixed to a diaphragm which conveys vibrations to a crystal; compression of the crystal produces currents which can be amplified and recorded on an oscilloscope, thus giving a tracing of the actual mechanical movements of the vocal fold.

Rhythmical stimulation of the recurrent nerve of one side showed that a rate of 90 stimuli per second caused vibration of the muscle at the same rate: a similar result was recorded at 100 C/S, although at this rate the clonic contractions were much smaller in amplitude. At 110 shocks per second no clonic movements occurred (Fig. 5).

To make certain that the apparatus was capable of recording higher rates of vibration, the tip of the transducer was placed in contact with the diaphragm of an earphone, which was made to vibrate at various frequencies.

The transducer was found to record accurately oscillations at rates of 250 and even 900 C/S (Fig. 6).

The evidence of comparative anatomy, of mechanical experimentation and of investigation by various electrophysiological methods leads to the conclusion that the clonic theory is untenable.

149 HARLEY ST.

LXV

MALIGNANT LYMPHOMAS OF THE PHARYNX

STANTON A. FRIEDBERG, M.D.
ROBERT H. EDWARDS, M.D. (by invitation)
GEORGE M. HASS, M.D. (by invitation)
CHICAGO, ILL.

An analysis of the clinical and pathological data on ten patients with malignant lymphomas of the nasopharynx and pharynx is contained in a previous report.[1] Further observations on several of these patients and six additional cases form the basis for this communication.

SUMMARY OF PREVIOUS OBSERVATIONS

Though the presenting symptoms of patients with malignant lymphomas of the pharynx are frequently confined to this area, these local manifestations are but one phase of a systemic affliction. Only rarely does the disease remain localized and, when it does, the diagnosis must be reconsidered. However, predictability of dissemination to other parts of the body on the basis of microscopic interpretation of pharyngeal biopsies alone is difficult. A more valuable prognostic sign would appear to be the duration of remission which follows initial diagnosis and treatment.

The term malignant lymphoma refers to a complex group of presumably neoplastic disorders which includes various types of lymphosarcoma, as well as Hodgkin's disease. It is convenient to attempt to classify each case but one is often impressed with the lack of any sharp distinction between different types of malignant lymphomas.[2] Although we specified follicular, lymphocytic, lymphoblastic, reticulum cell and Hodgkin's types of malignant lymphoma in our previous

From the Departments of Otolaryngology and Pathology, Presbyterian Hospital, Chicago, Illinois, in affiliation with the University of Illinois College of Medicine.

report, it was noted that microscopic features of several types might be present in different organs or at different times in any given case. One is thus led to suspect that the various types represent variants of the same process. Since there may be considerable disagreement among pathologists as to the dominant cell type in any given case, it has been suggested that the entire group be simply designated as lymphosarcoma. We prefer the term malignant lymphoma.

If, as rarely occurs, a malignant lymphoma does not manifest itself subsequently in other areas, one may justifiably conclude that it represented a single isolated focus of disease or an error in diagnosis. The reticuloendothelial reaction to infection (particularly in the pharynx) and true neoplasia are occasionally indistinguishable. More often, however, isolated foci appear at varying intervals in other areas and, since the routes of spread are not the customary ones for metastatic neoplastic disease, one is led to the conclusion that multicentric foci of origin are implicated in the pathogenesis of the lymphomas.

Clinically, it is impossible to distingush between the various forms of malignant lymphoma arising in or having their primary manifestations in the pharynx.

The sensitivity of malignant lymphomas to therapy with irradiation is well-known. Large tumors often begin to recede following treatment with as little as 800 r and complete local dissolution may be anticipated with relatively low total dosage. Repeated irradiation and the use of newer chemotherapeutic measures for disseminated disease are effective controls for varying intervals.[3] Eventual lack of response is to be expected, however, and occasionally the measures employed in the control of the disease may result in undesirable tissue alterations which are responsible for a fatal outcome.

In the last analysis, we are dependent upon the continued microscopic examination of tissue and correlation of this with the patient's clinical history for an accurate evaluation of any given situation. Unfortunately this may not be forthcoming until the disease has run its course or the intensive therapy has had too many undesired effects on normal tissues.

Fig. 1.—(Addendum II, Case 3 in previous series.) Tumor involving left lateral pharyngeal wall. Malignant lymphoma, lymphoblastic type.

SUBSEQUENT COURSE OF THREE PATIENTS PREVIOUSLY REPORTED

Addendum I. In our previous report, Case 2 was that of a 55 year old woman with an enlarged left tonsil and a solitary cervical node on the same side. The microscopic diagnosis rested between an abnormal response to infection and malignant lymphoma of the lymphoblastic type. X-ray therapy was successfully employed. She was kept under observation and remained well for almost five years, at which time an enlarged node appeared in the right axilla. This was removed and found to represent a typical malignant lymphoma of the Hodgkin's type. In reviewing the biopsy of the tonsil, it was still impossible to make a diagnosis of Hodgkin's disease although certain clues indicated that such a diagnosis might be seriously considered.

Nasopharyngeal obstruction by lymphoid tissue caused symptoms one year later. This was soon followed by a cervical enlargement on the right side which was diagnosed in Germany as Hodgkin's disease. A left supraclavicular mass, enlargement of the liver and spleen and worsening of her general health became evident in April, 1957. She has received three courses of nitrogen mustard therapy and appears to be in poor condition at this time, nearly six years after the onset of symptoms.

Comment. Almost all authors have mentioned the variability of the histopathologic pattern between different areas of disease in the same patient. The interrelationship of Hodgkin's disease and other lymphatic tumors has been described by Custer and Bernhard.[4] In this particular instance, the reactions of severe chronic inflammatory disease, lymphoblastic lymphosarcoma and Hodgkin's disease can all be identified in the available material.

There is wide variation in the course of malignant lymphomas in different patients.[5] The initial remission of five years in this case is of interest. Whether longer survival is to be expected in females with Hodgkin's disease has been a subject of controversy. The course of this female patient can be contrasted with that of a male with Hodgkin's disease of the tonsil who lived but two months from the onset of his difficulty.[1]

Addendum II. A 73 year old man (Case 3 in our previous report) had a malignant lymphoma of the lymphocytic type involving the left lateral pharyngeal wall (Fig. 1). The possibility was entertained that the process might be benign. Four and one-half years later, a node appeared in the right supraclavicular area and was diagnosed as lymphosarcoma. An exploratory laparotomy revealed gastric involvement by lymphosarcoma. He received x-ray treatment to the abdomen. One year later, nodes appeared in the right cervical region and these were also treated. The microscopic diagnosis at this time was Hodgkin's disease. He is now 80 years old and has lived for six years since the original diagnosis, there having been an initial remission period of four and one-half years.

Comment. In both this case and the preceding one there were elements in each initial biopsy which suggested a reaction to inflammation. In each instance it was anticipated that the true nature of the process would only become evident with the passage of time and in each instance new foci of disease did not appear for almost five years. The optimism which existed during this period has been dispelled by subsequent events since, in both cases, the original opinions of malignant lymphoma of the lymphocytic and lymphoblastic types have now been changed to malignant lymphoma of the Hodgkin's type in subsequent biopsies from other locations.

Addendum III. A 40 year old man (Case 10 in our previous report) had an undifferentiated malignant lymphoma (reticulum cell type) of the pharynx. Shortly after initial treatment of this malignancy, he developed intestinal obstruction for which resection of an intestinal lesion was performed. This lesion was diagnosed as a malignant lymphoma (reticulum

cell type). A diffuse retroperitoneal nodular tumor was also noted at operation. He received x-ray therapy postoperatively and has remained free of disease for the past four and one-half years.

Comment. The anaplasia of this patient's tumor was regarded as an extremely poor prognostic sign, as was the short remission period following the original diagnosis. Nowhere do we see better proof of the unreliability of immaturity of cell type as a basis for absolute predictability of the future behavior of malignant lymphomas. Prognosis in individual cases is extremely difficult to determine by microscopic methods and Hall and Olson have aptly questioned whether the histologic diagnosis made by the pathologist has any significance other than to establish the diagnosis of malignant lymphoma.[5]

REPORT OF ADDITIONAL CASES

Malignant Lymphoma, Reticulum Cell Type

(three patients)

CASE 11. F.C., a 96 year old white male, was seen at Presbyterian Hospital in April, 1954. Despite his age, this was his first hospital admission and the reason given was shortness of breath. On the evening before admission a doctor had made a diagnosis of a left peritonsillar abscess and had attempted to incise the mass. This brought on an acute episode of obstructive dyspnea, for which a pulmotor squad was summoned.

When seen at the hospital, he had respiratory obstruction due to a huge mass occupying the oropharynx and extending outward into the mouth (Fig. 2). There was a recent wound on the superior lateral surface of this mass. An emergency tracheotomy was performed. Several days later, with gas anesthesia administered via the tracheostomy, a biopsy of the left tonsil was performed. The sections revealed a malignant lymphoma of the reticulum cell type. There were no enlarged lymph nodes. The liver and spleen were not enlarged.

X-ray therapy was administered and before the patient had received 1000 r the tonsillar mass had begun to shrink. He received 2000 r. The tonsil became atrophic and he was well until December, 1954, when he developed a painless node in the right axilla. This was also treated with x-ray therapy (1800 r). The patient seemed well for his 97 years but gradually weakened and died at home on April 3, 1955, one year from the date of diagnosis. No autopsy was obtained.

Microscopic Study: The material consists of several pieces of tissue removed from the right tonsil. These fragments are partly covered by stratified squamous epithelium. Beneath the epithelium there is a mass of lymphoid tissue which has no discrete follicular structure. There are a few circumscribed areas which seem to represent either remnants of pre-existing lymphoid follicles or demarcated hyperplastic follicular structures which have little resemblance to normal lymphoid follicles. There are a few residual islands of lymphoid tissue in some fragments but

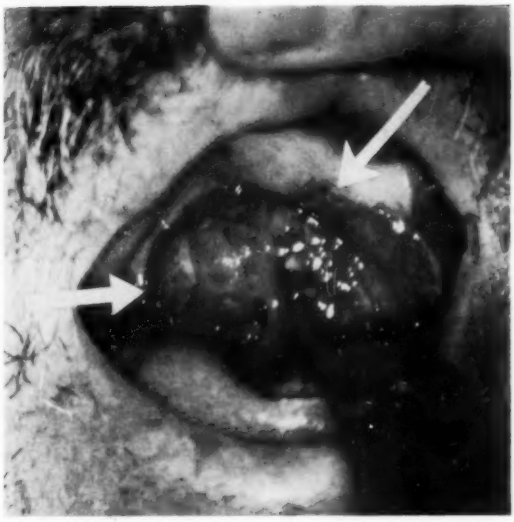

Fig. 2.—(Case 11) Left tonsillar mass filling entire oropharynx. Upper arrow points to site of incision made elsewhere for "peritonsillar abscess." Reticulum cell sarcoma.

most of each fragment is composed of large immature cells in which the nucleus occupies the principal part of the cell structure. The nuclei are round with occasional indentations. Nucleoli are prominent. Mitotic figures are common. The cytoplasm is not conspicuous. The cells are distinct from one another and do not occur in sheets or in any regular formation. The dominant cell type resembles a very immature reticulum cell and it would seem proper to classify the tumor as a malignant lymphoma of the reticulum cell type.

Comment. Despite the size of the tumor there was no gross ulceration. The appearance microscopically is that of a highly malignant form of reticulum cell sarcoma. Due to the advanced age of the patient, no conclusions can be drawn regarding survival rate. Comparison with the case recorded in Addendum II, and with others of the reticulum cell type described previously, would again point to the undesirability of depending too much on the type of cell as an absolute basis for prognosis.

CASE 12. L.G., a 35 year old German, had been in the United States for ten weeks prior to admission to the Out-Patient Clinic at Presbyterian Hospital in April,

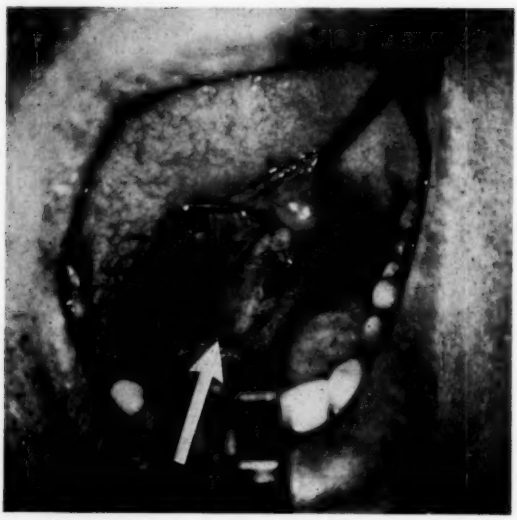

Fig. 3.—(Case 12) Infiltration of right posterior tonsillar pillar by tumor mass which extends into nasopharynx. Reticulum cell sarcoma.

1955. Fourteen months previously he had a gastric resection in Germany for peptic ulcer. (A detailed report of the microscopic study was obtained and there was no indication of lymphoma.) Four months ago he had undergone surgery for relief of nasal obstruction. He had noticed impairment of hearing in the right ear for six weeks and for five weeks he had been conscious of a swelling in the right side of this throat and a change in his voice. In the two weeks before seeking medical attention he had chills and fever, progressive difficulty in swallowing and inability to breathe while lying down because of the obstruction in his throat. There had been loss of appetite and a loss of 25 pounds of weight in three months.

On examination, the pulse, blood pressure, respiration and temperature were normal. His weight was 152 pounds. The principal findings were limited to the pharynx where a bulge of the right half of the soft palate was continuous with a swelling lateral to the right tonsil. The right tonsil was displaced medially. There was infiltration of the right posterior tonsillar pillar and a larger mass almost filling the nasopharynx (Fig. 3). No ulceration was observed. There was fluid in the right tympanum. There was no lymph node enlargement. The liver, spleen and kidneys were not palpable. Chest x-ray was negative. The hemogram was normal. A biopsy of the mass behind the right tonsil was made. The microscopic diagnosis was malignant lymphoma of the reticulum cell type.

The patient was referred for irradiation therapy and received 2700 r to the pharynx. Following this, the nasopharynx and oropharynx were entirely clear.

On August 2, 1955, he was admitted to the hospital because of continued weight loss, nausea and anorexia. There was mild anemia with a normal differential count. Blood chemistry tests were normal. He was given a high caloric diet and discharged in three days.

He was again seen on August 18, 1955, with a complaint of left lumbar pain. An intravenous pyelogram disclosed a mass displacing the left kidney downward and laterally. Gastric fluoroscopy showed an extrinsic mass compressing the fundus on the lesser curvature. X-ray therapy to the abdomen was instituted and he received 1700 r. His weight at this time was 126 pounds, representing a loss of 26 pounds since admission in April, 1955.

In late September, 1955, a mass measuring 3 x 3 cm was evident in the right femoral triangle. He had pain over the lower thoracic spine and pelvis, although no lesions of bones were observed on roentgenograms. X-ray treatment (1000 r) relieved this pain.

On November 1, 1955, x-rays disclosed left pleural effusion with marked mediastinal widening. He was dyspneic and stated that pain was present in the left upper abdomen. His ankles were swollen and he had been coughing up blood for three days. Anemia was marked (Hb., 7.6 gm %, and an erythrocyte count of 2,340,000). Neurological examination disclosed the possibility of left cerebellar involvement. He was given Meticorten without improvement and this was followed by nitrogen mustard therapy. Repeated thoracenteses were done to remove fluid from the left pleural cavity. His weight diminished to 112 pounds. Episodes of abdominal pain were frequent. There was progressive enlargement of the mass in the left upper abdomen. Narcotics were used to control severe pain. The bone marrow was normal except for changes due to therapy. He became progressively weaker and died on December 2, 1955, seven months after the diagnosis of malignant lymphoma was made and approximately eleven months after the onset of initial symptoms.

Microscopic Study. A section of tissue removed from behind the right tonsil reveals a covering of stratified squamous epithelium which is infiltrated by polymorphonuclear leukocytes and large cells resembling neoplastic reticulum cells. There is no demarcation between the epithelium and the underlying tumor. The epithelial penetration by neoplastic cells is quite different from that often encountered in tumors arising from epithelium in this region and which are usually designated as transitional cell carcinomas or lympho-epitheliomas. There is no trace of lymphoid structure in the main mass of tumor which consists of cells varying greatly in size and shape. The cells have large nuclei. Mitotic figures are common. The cytoplasm is voluminous and weakly stained. The cells do not occur in sheets or any other specific arrangement except that they are not adherent to one another. The dominant cell type closely resembles a malignant reticulum cell and the tumor is classified as a malignant lymphoma of the reticulum cell type.

Necropsy. The pathological diagnoses included malignant lymphomatous involvement of the mediastinal and peri-aortic lymph nodes, the left lung, liver, spleen, diaphragm, pericardium, adrenal glands and the stomach. In the stomach there was extensive involvement with evidence of the previous partial gastrectomy. The only organs not involved were the brain, kidneys, pancreas, thyroid, parathyroid and bone marrow. The cytology was that of a malignant lymphoma of the reticulum cell type.

Comment. This case illustrates a rapidly-developing systemic disease which appeared first in the pharyngeal area. Treatment was not effective. At no time was there evidence, other than anemia, of any abnormality of the hematopoietic system. All factors which account for the variable course of these diseases are not known but the variability is often vaguely attributed to "varied virulence," "evolutionary form" and "inherent quality of the disease."[5] This patient did not exhibit any of the sequelae which often follow the administration of suppressive therapy, possibly because of his relatively short survival. It is more likely that this patient had severe generalized unrecognized internal lymphomatosis when first seen. Certainly, the degree of involvement of vital internal organs, though often unknown, is more important in prognosis than almost anything else.

CASE 13. E.N., a 45 year old male, had severe nasal obstruction and right-sided headaches for several months prior to the onset of intermittent double vision. He was examined by his family physician in early January, 1957. Between January 19 and January 30, there was progressive loss of vision in the right eye so that only light perception remained. He was admitted to a suburban hospital where a submucous resection and rhinoplasty were performed on January 30. According to the reports, he seemed improved for several days but then experienced further deterioration of vision with the additional development of unilateral right exophthalmos and ophthalmoplegia. Roentgenograms taken at this time were "inconclusive."

According to information received, ten days later an external approach to the ethmoid area was undertaken and a large amount of polypoid tissue was encountered. Apparently there was destruction of bone in the ethmoid and sphenoid regions. Microscopic diagnosis of the tissue was "markedly inflamed nasal polyps." The patient was reported to have improved slightly after the second operation but improvement was of short duration.

At about this time a swelling occurred at the site from which a right lower molar tooth had been extracted. The swelling was accompanied by enlargement of a lymph node overlying the right submaxillary gland. A biopsy of the alveolar swelling was taken and all the previous material was reviewed. It was decided that the patient had a malignant process, probably primary in the nose, with metastases to the sinuses and that the lesion was a malignant melanoma.

The patient was then transferred to Presbyterian Hospital under the care of Dr. D. P. Slaughter who asked one of us to see him. The pain was such that the patient required sizeable narcotic dosage every four hours. There was proptosis (4 mm), ophthalmoplegia and complete optic atrophy of the right eye. Intranasal examination was negative but there was a large mass in the nasopharynx. Swelling of the right first molar area, a large lymph node in the right submaxillary area, and a right serous otitis media were other physical findings. The hemogram, chest x-ray and chemical analyses of the blood were normal.

Biopsy of the nasopharyngeal mass was interpreted as a malignant lymphoma of reticulum cell type. X-ray therapy was undertaken and after approximately 800 r had been given there was marked improvement. He received an estimated

2000 r to the pharynx. The proptosis disappeared and ocular mobility but no vision returned. No medication was required for pain.

Several weeks later a palpable mass appeared lateral to the healed external ethmoidectomy incision on the right side. This region was also treated by irradiation with prompt regression following 1200 r. A right peripheral facial paralysis developed in April, 1957, followed by weakness of the left arm and leg. Steroid therapy (Meticortelone®) was started at this time.

Microscopic Study. A section of the biopsy from the mass in the nasopharynx is almost entirely composed of neoplastic tissue partly covered by normal ciliated respiratory epithelium. The epithelium extends into the neoplastic tissue in small crypts. The tumor is uniformly cellular with very little stroma. There are no lymphoid follicles nor are there any areas in which lymphocytes are abundant. The principal cell of the tumor is large with a prominent nucleus and relatively little cytoplasm. The nucleus is irregular and often has indentations. Nucleoli are large. Mitotic figures are numerous. Eosinophils are uniformly distributed throughout the tumor. There is no necrosis. No typical Reed-Sternberg cells are encountered. This tumor is perhaps best classified as a malignant lymphoma of the reticulum cell type. It might be regarded as a Hodgkin's type of malignant lymphoma because of the large number of eosinophils, but there are no other features of Hodgkin's disease.

Comment. It would seem that this patient's primary lesion must have been in the nasopharynx, with subsequent rapid spread to the ethmoid, sphenoid and orbital areas. Involvement of the cranial nerves followed thereafter. Local rather than systemic extension will doubtless cause the patient's expected demise and this is the first example of such a mechanism in the entire series. In all other instances the pharyngeal growth has vanished rapidly after treatment and has not reappeared either at or near the original site.

Another feature of this case is the lack of clear microscopic distinction between reticulum cell sarcoma and Hodgkin's disease. This difficulty in diagnosis is often more apparent to the pathologist than to the clinician.

Malignant Lymphoma, Lymphoblastic Type

(two patients)

CASE 14. I.A.S., a 56 year old negress, was first seen in May, 1950, with a skin condition thought to be atopic dermatitis. One year later a diagnosis of marked hypertrophy and chronic infection of the tonsils was made. On several subsequent occasions she was seen with acute tonsillitis and recurrent swelling of both parotid glands. Her clinic attendance was irregular and several appointments for tonsillectomy were broken. Weight loss, generalized arthritis, a persistent skin eruption and mild cardiac decompensation were noted. Chest roentgenograms were negative. Hemograms were normal.

Tonsillectomy was performed in April, 1952, for the relief of marked pharyngeal obstruction and recurrent tonsillitis. Although histological examination had been requested, tissue was not sent to the laboratory from the operating room. The patient was seen repeatedly because of intermittent, recurrent, bilateral, parotid enlargement. Sialograms were normal. She had atrophic rhinitis with associated crusting and tentative clinical diagnoses included Boeck's sarcoid, Mikulicz's syndrome and lymphosarcoma.

The nasopharynx was examined with negative results. The blood count showed a reversal in the usual polymorphonuclear-lymphocyte ratio.

In September, 1953, abnormal nasopharyngeal tissue appeared along with a solitary axillary lymph node. From biopsies of these, a diagnosis of malignant lymphoma of lymphoblastic type was made in each instance. Recurrent parotid and submaxillary gland enlargement, dry mouth, purulent nasal discharge and persistent skin eruption led to her hospitalization in October, 1953. At this time the blood count showed 10 gm per cent of hemoglobin, an erythrocyte count of 3,400,000 and a leukocyte count ranging from 7,000 to 9,000 with 31 per cent neutrophils, 64 per cent lymphocytes and no abnormal cells. A weight loss of 60 pounds in two years was recorded. Anterior and posterior cervical, inguinal and axillary adenopathy was noted. No mediastinal involvement was evident. Bone marrow studies disclosed lymphocytosis consisting of mature lymphocytes. X-ray therapy to the enlarged lymph nodes was instituted. This was followed by a course of triethylene melamine (30 mgm over a three week period).

Her appearance at the clinic during 1954 was irregular. Fatigue, loss of appetite, loss of hair and pain in the parotid regions were prominent symptoms. In August, 1954, she complained of headache, chest pain, diarrhea and vomiting. Roentgenograms of the chest and intestinal tract were normal. She entered Cook County Hospital on October 10, 1954, and expired several days later, four and one-half years after her initial clinic visit and one year after a definitive diagnosis had been established.

Microscopic Study. Tissue removed from the nasopharynx contains many immature cells with large nuclei and abundant cytoplasm. There are a few eosinophils and occasional hyperchromatic reticulum cells suggestive of Reed-Sternberg types. Some parts of the tumor might be regarded as a malignant lymphoma of the reticulum cell type, other parts as lymphoblastic type and other parts as Hodgkin's type. The predominant cell is an immature large lymphocyte.

Microscopic study of axillary lymph nodes shows obliteration of normal structure by large numbers of lymphoid cells which are closely packed together. There is no trace of lymph sinuses. There are many mature lymphocytes between which there are occasional large atypical reticulum cells. In some areas eosinophils are numerous and there are other small areas of necrosis. The large reticulum cells at times resemble Reed-Sternberg cells. The diagnosis would seem to rest between malignant lymphoma of the Hodgkin's or lymphoblastic types.

Necropsy. The patient died of pneumococcal meningitis, secondary to subacute pneumococcal mitral and aortic endocarditis. The spleen, liver and genito-urinary organs were the site of lymphosarcomatous infiltration.

Comment. The initial clue to this patient's illness was the sudden appearance of marked tonsillar hypertrophy of sufficient degree to

cause pharyngeal obstruction. An unfortunate delay in diagnosis resulted from failure to obtain microscopic study of these structures, as had been requested, or of the skin. Evidence of mild systemic involvement, however, can be assumed to have been present from the onset of symptoms and took the form of skin eruption (a common manifestation of malignant lymphomas), weight loss and persistent infections. By the time the diagnosis was made on biopsies of nasopharyngeal tissue and axillary lymph nodes, there was a reversal of the polymorphonuclear-lymphocyte ratio and this persisted throughout the remainder of the patient's life. Although a frank picture of lymphatic leukemia was not apparent, this may at times be associated with any type of malignant lymphoma.[2] This is the only instance in our series of an abnormal blood finding other than anemia and this finding is of no diagnostic significance.

Features common to lymphoblastic, reticulum cell and Hodgkin's types of lymphoma were found in examination of the material from this patient, again lending further evidence to the theory that these tumors share a common origin.[2,3,5,6] Relations among these processes to mycosis fungoides or the Mikulicz syndrome should also be emphasized in connection with this patient's clinical course.

CASE 15. W.B., a 59 year old housewife, was first seen by Dr. L. J. Wallner in January, 1957. Nasal obstruction, present for one year, had increased in recent months. On examination the nasal passages and sinuses appeared normal. The nasopharynx was filled with a mass resembling lymphoid tissue (Fig. 4). The oropharynx and larynx were normal, as were the tympanic membranes. The hemogram was normal.

Employing local anesthesia, nasopharyngeal tissue was removed with punch forceps. A frozen section diagnosis of "lymphoid tissue" was made. Paraffin sections, however, were interpreted as representing a malignant lymphoma of the lymphoblastic type.

The patient received, elsewhere, approximately 4500 r through two portals of 8 x 20 cm to the nasopharynx and cervical region. This resulted in disappearance of the residual nasopharyngeal enlargement. She is now being observed at monthly intervals for evidence of local or systemic disease.

Microscopic Study. The material consists of several fragments of tissue partially covered by squamous and a ciliated respiratory type of epithelium. The tissue is lymphoid in character with scattered lymphoid follicles. The follicles are, as a rule, quite large and not sharply demarcated from the cells which lie between them. The follicle cells are abnormal, being intermediate in size between the large reticulum cells normally found in the center and smaller lymphoid cells at the periphery of follicles. There is a tendency for the cells to be multi-angular, with nuclei slightly larger than those of normal lymphocytes. The cytoplasm is scanty

Fig. 4.—(Case 15) Mirror view of nasopharynx showing tumor mass of sufficient size to occlude both choanae. Malignant lymphoma, lymphoblastic type.

and mitotic figures are not numerous. Cells of this type have completely replaced normal lymphoid tissue in many areas. Judging from the predominant cell type, this malignant lymphoma is best classified as a lymphoblastic type.

Comment. It has been stated that the only two histological pictures likely to cause problems in the differential diagnosis of malignant lymphoma are those of severe chronic inflammation on the one hand and highly anaplastic carcinoma on the other.[7] Difficulty also may arise in dealing with leukemias, small-cell sarcomas, infectious mononucleosis, conspicuous hyperplasias and other processes. It becomes increasingly difficult in frozen sections which, in this instance, were done and incorrectly interpreted. It is too early in the course of this patient's illness to render a prognosis. The fact that she had localized symptoms for one year prior to diagnosis may be a favorable sign with respect to any immediate prospects of recurrence. The eventual prognosis, however, must be guarded since all available

Fig. 5.—(Case 16) Large non-ulcerated mass occupying right tonsillar fossa, almost entirely occluding oropharynx. Arrow points to only remaining communication between mouth and pharynx. Malignant lymphoma, lymphocytic type.

evidence indicates that, sooner or later, other parts of the body will become involved.

Malignant Lymphoma, Lymphocytic Type

(one patient)

CASE 16. A.J., a 53 year old Lithuanian immigrant, began to notice tightness in his throat several months prior to admission. He had had two febrile episodes with temperature of 103 F., with chills and sweating. He had a poor appetite for three weeks prior to admission and a 12-pound weight loss in the past nine months. He was first seen in September, 1955, at which time the enlargement in his throat interfered with swallowing and talking. Examination revealed a large, reddish non-ulcerated mass occupying the right tonsillar fossa and almost occluding the pharynx (Fig. 5). The liver, spleen, lymph nodes and kidneys were not enlarged. The hemogram was normal. A tentative diagnosis of lymphoma of the right tonsil was made and excision biopsy of the mass was done. The pathologic diagnosis was malignant lymphoma of the lymphocytic type. He received roentgen therapy to

the involved area. He has been observed at monthly intervals since and, as of March, 1957, has had no local or systemic evidence of recurrent disease.

Microscopic Study. There is a large, well-circumscribed mass of lymphoid tissue covered over more than one-half of its circumference by stratified squamous epithelium. The epithelium is demarcated from the lymphoid tissue by a layer of dense fibrous tissue infiltrated with cells of lymphoid type. The main mass of tissue is uniformly composed of small cells which are not arranged in follicles. These cells are a little larger than normal lymphocytes. Their nuclei tend to be round or slightly indented and surrounded by a thin rim of pale eosinophilic cytoplasm. Mitotic figures are numerous. There are no lymphoid sinuses and very little stroma. The dominant cell type is similar to cells ordinarily classified as abnormally large lymphocytes so that this should be diagnosed as a malignant lymphoma of the lymphocytic type.

Comment. This patient has had a remission of eighteen months since initial diagnosis and treatment. One other patient, an elderly male with a lymphocytic lymphoma, lived four and one-half years before he developed systemic disease (Addendum II). A female, aged 57, with similar histological findings died as the result of disseminated lymphomatosis within a two-year period. Thus, prognosis based only upon similarity of cell types in different patients is no more dependable than predictions based upon age, sex or postulated degree of malignancy of a particular tumor. The most important unknown factor which influences prognosis in most cases would seem to be the degree of systemic involvement in vital areas not readily subjected to well-guided treatment.

RESUMÉ

Although numerically this represents a small series, certain facts stand out. It will be noted that there are 8 males and 8 females and that the age span is from 6 to 96 years (Table I).

Of the 15 determinate cases, 9 are deceased and 3 living with evidence of disease are not expected to survive much longer. Three patients are living without evidence of disease, one only three months after diagnosis and another at 18 months. Only pessimistic predictions can be made in these two cases. The third patient, after experiencing a recurrence ten months after diagnosis, has remained free of disease for four and one-half years.

The histological type of malignant lymphoma has no particular prognostic significance except that the giant follicular type is alleged

TABLE I

MALIGNANT LYMPHOMA OF PHARYNX

RESUMÉ OF 16 CASES

TYPE OF MALIGNANT LYMPHOMA	CASE NO;	AGE AT ONSET	SEX	INITIAL PERIOD OF REMISSION (MONTHS)	LIVING WITH EVIDENCE OF DISEASE (MONTHS)	LIVING WITHOUT EVIDENCE OF DISEASE (MONTHS)	DEAD DURATION OF DISEASE (MONTHS)
Giant Follicular	1	19	F	?	?	?	?
Lymphocytic	3	73	M	56	76	..	..
	4	57	F	0	.	.	24
	16	53	M	?	.	18	..
Lymphoblastic	5	6	M	0	.	..	6
	14	56	F	17	..	..	52
	15	59	F	?	.	3	..
Hodgkin's	6	70	M	0	.	..	2
	2	55	F	52	66	..	..
Reticulum Cell	7	44	F	60	.	.	125
	8	47	F	10	.	..	15
	9	35	F	0	.	..	21
	10	40	M	10	.	54	..
	11	96	M	8	.	..	12
	12	35	M	0	.	..	11
	13	45	M	0	5	..	..

to have the best outlook. Our only patient with a malignant lymphoma of the follicular type cannot be located at this time.

The series is too small to draw any conclusions regarding the relative incidence of the different forms of malignant lymphoma. Such wide variation is to be found in the literature that one must assume it to be due to different standards and methods of classification.

Perhaps the most obvious conclusion to be drawn from Table I is that the initial period of remission seems to be the only prognostic sign of significance. (There is one exception to this statement.) The three patients with the longest survival time to date (125, 76 and 66 months) had initial remission periods of 60, 56 and 52 months respectively.

Of the 6 patients who showed signs of generalized disease soon after diagnosis by pharyngeal biopsy, none lived more than two years and some were dead in a very few months.

We feel that the best summary of this situation is to be found in the opening paragraph of an excellent article by Hall and Olson concerning 115 patients with malignant lymphomas of all types:[5] "The course of a malignant lymphoma varies widely from patient to patient. Some patients do not respond to any therapy and die within a few months. Many have remissions of a few months, respond less and less with future therapy, and die in from two to three years after the diagnosis is made. Some have a course similar to that of the latter group but remissions are longer, spread of the disease is slower, and they live five, ten or 15 years. In some cases these patients have a long remission from a single course of therapy and then show a rapid downhill course. Other long survivors have shorter single remissions but continue to respond to treatment for years. A few patients will remain apparently free of disease for periods of up to 25 years and then relapse and die of their disease. In some instances, especially with visceral tumors of the lymphosarcoma group, there appears to be a complete cure. A comparison of the series of untreated cases of Minot and Isaacs with the many reports of treated cases indicates that the basic course of these diseases is the same with or without therapy." To this we would like to add one note of possible optimism for the future; namely, that current therapy, if carried out vigorously, may

and often does eliminate all microscopic evidence of the disease but unfortunately the locus and amount of therapy required to do this under present conditions is sooner or later lethal to the patient. Future prospects for cure under slightly improved conditions, therefore, seem good.

DIFFERENTIAL DIAGNOSIS

As previously mentioned,[1] the finding of any abnormal or recurrent mass of lymphoid tissue in the nasopharynx, of a smooth unilateral swelling of the lateral pharyngeal wall, or of a unilateral tonsillar hypertrophy, with or without ulceration, should arouse suspicion of malignant lymphoma. Actually, the largest tumors and the majority of tumors we have encountered have had smooth, non-ulcerated surfaces.

Among the inflammatory conditions, peritonsillar abscess was diagnosed in two patients before admission and Harman et al. have indicated the same error in three patients in their series.[7] With the widespread use of antibiotics, peritonsillar suppuration may become encapsulated and persist in the form of a sterile accumulation with tonsillar displacement. Retropharyngeal abscess, pharyngomaxillary space infection, infectious mononucleosis and Vincent's infection should also be ruled out.

Among the chronic inflammatory conditions, tuberculosis of the cervical vertebrae and tuberculous cervical adenitis may cause a uniform smooth pharyngeal swelling. Tuberculosis of the nasopharynx, pharynx and tonsil should be kept in mind. The reactions of severe chronic non-specific inflammation or hyperplasia may be difficult to distinguish from actual lymphomatous infiltration.

There are a number of tumors arising in the pharynx which may grossly resemble malignant lymphomas. Among these are tumors of minor salivary gland type, adenocarcinomas, lympho-epitheliomas and undifferentiated carcinomas.

Neurofibromas of the cranial nerves—often referred to as schwannomas or neurilemmomas—can simulate malignant lymphomas, particularly when the vagus nerve is involved. We have observed several instances where such a diagnostic problem arose. Chordomas,

plasmacytomas and carotid body tumors should also be included in the differential diagnosis.

Differentiation of the lymphoid disorders themselves poses the greatest problem and the histological difficulties attending these decisions have been mentioned repeatedly. From a clinical standpoint there are no features which, without exception, will permit differentiation of tuberculous lymphadenitis, Hodgkin's disease, lymphosarcoma, aleukemic lymphatic leukemia, lympho-epithelioma and even undifferentiated carcinoma.[8]

SUMMARY AND CONCLUSIONS

An analysis of six additional patients with malignant lymphomas of the pharynx, when added to a previous study, has brought the total number in the present series to 16. The first symptoms in each case were referable to the pharyngeal or nasopharyngeal area.

Despite the initial localization of symptoms and findings, the pharyngeal manifestations were but transitory evidence of a widespread lymphatic disorder which was almost uniformly fatal after varying periods of time.

The term malignant lymphoma refers to a group of disturbances which includes the various types of lymphosarcoma as well as Hodgkin's disease. Included in this series are one patient with giant follicular lymphoma, three patients with lymphosarcoma of the lymphoblastic type, three patients with lymphosarcoma of the lymphocytic type, two patients with Hodgkin's disease and seven patients with reticulum cell sarcoma.

The difficulties in microscopic classification of malignant lymphomas were emphasized. It was frequently possible to detect features common to more than one type of lymphoma, as well as transitions from one form to another in the same patient.

Prediction of the clinical course on the basis of the histologic picture was not dependable. The clinical course of the disease varied as widely as the microscopic type, and there was no consistent correlation between the two.

Systemic involvement usually appeared soon after the diagnosis of the pharyngeal lesion was made. Survival among such patients was usually only a few months and rarely exceeded two years.

An initial lengthy period of remission usually implied a longer survival. The three patients with the longest periods of survival had first remissions of 60, 56 and 52 months.

There were 15 determinate cases. Nine died of the disease. Three are living with evidence of progressive generalized disease. Of the three living without evidence of the disease, two are of such recent date that no conclusions are pertinent, while one is in a second period of remission which has now lasted 52 months.

X-ray therapy and chemotherapy were effective in controlling the disease for varying periods but had no curative value.

The final evaluation in any given patient with malignant lymphoma was usually not possible until the disease had run its course.

122 So. Michigan Ave.

The authors wish to express appreciation to Dr. L. J. Wallner, Maria E. Ikenberg and Louis S. Pedigo for their photographic assistance.

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LXVI

THE ROLE OF RHINOLOGY IN PITUITARY SURGERY

Oscar Hirsch, M.D.

Boston, Mass.

It is 50 years ago, almost to the day, that the first transsphenoidal operation was performed on May 23, 1907. One year previously the idea of operating on the pituitary was considered fantastic. But pituitary tumors existed and were diagnosed. Their treatment consisted of trepanation of the skull and decompression. About a dozen operations were performed by Horsley in 1904,[1] using the cranial method, but 40 per cent of the patients died and the rest remained crippled. The first transsphenoidal operation was performed by the surgeon Schloffer[2] by way of temporary displacement of the external nose. When I witnessed such an operation by Eiselsberg it occurred to me that this operation could be done by a rhinologist with less mutilation outside and inside the nose and also with less risk. At that time there happened to be a patient on the ward of the Department of Neurology in Vienna who had lost his eyesight and was in a desperate condition. I suggested an endonasal exploratory operation on this patient to the Chief of the Department, Dr. von Wagner-Jauregg. When it came to the operation I used the ethmoidal access[3] to the sphenoidal cavity. I found a cystic tumor, the patient fully regained his sight. From this time on I was entrusted with the operations on pituitary tumors in the Allgemeine Krankenhaus of Vienna. In all other cases I used the septal[4] method. By submucous resection of the septum, cartilage and bone were removed. It was then possible to spread the flaps to the width of both nasal cavities and reach the anterior walls of the sphenoid and expose the entire width of both sphenoidal cavities. They were pierced at the thinnest point and from this breach the walls of the sphenoid were removed by punches. The enlarged sella became visible. The operation is carried out in a newly created, wide tunnel which is separated from the nasal cavities by the flaps, thus restricting possible infection. In some cases the sella had to be opened by chisel, in others defects in

the floor of the sella were found from which the bony sella was removed. At this point the instruments were freshly sterilized, the operating table was again covered with sterile linen. The dura was incised and excised and from this defect the tumor was removed by curette and suction. This method of suction, which is now common in surgery, was used by me instead of the method which was prevalent at that time, namely, sponging the operative field with gauze strips. I felt that this method (i.e., suction) would prevent infection of the tumor. This method of suction also proved helpful postoperatively in cases of infection of the tumor. It was my impression that I was able to cure beginning meningeal symptoms due to infection of the tumor. Even now I do not rely solely on antibiotics when the first symptoms of meningitis appear, but I use suction in connection with the antibiotics.

After I began to use the septal method the mortality rate in pituitary tumors decreased.

There was still another factor which contributed to the greater safety of the operation. I operated upon the first 20 cases of pituitary tumor in the out-patients' section of the ear department. The patients were lying on the same ward as did patients who had suppurative diseases. When I could transfer patients for operations to the clean operating room of the eye department the incidence of infection decreased to 5 per cent and remained so up to the antibiotic era when it decreased to one loss among 75, i.e., 1.3 per cent.[5]

The rationale of the first transsphenoidal operation performed by Schloffer[6] was different from that of my own. To Schloffer's mind the risk of the operation was a cerebrospinal rhinorrhea; this did not keep him from operating, because in skull injuries he found that infection developed in only 13 per cent of the cases. That is why he ventured to perform the operation. I based the endonasal operation on the anatomical relation of the dura and pia-arachnoid. The pituitary is covered by dura only as far as the diaphragm.[7] The operation on the pituitary is therefore extradural. This anatomy pertains in cases of pituitary tumors to the lower segment[5] of the pituitary tumor which is the only segment in the field of operation. If the tumor expands into the cranial cavity the upper pole of the tumor becomes covered by the optic chiasm and by the circle of Willis.

Operative interference with this structure is, of course, hazardous and has to be strictly avoided. That brings us to the limitation of the operation.

From the operative standpoint we can divide all pituitary tumors into three categories:

1) Supradiaphragmatic tumors. These lie exclusively above the diaphragm within the cranial cavity, are real brain tumors and are not amenable to transphenoidal operation. They are recognized in x-ray by a normal sella.

2) In this category are the intrasellar tumors which develop within the sella and expand the sella exclusively or mainly toward the sphenoidal cavity; they are recognized in x-ray by the enlarged sella, the entrance of the sella remaining but little changed. Since the tumors do not expand into the cranial cavity they do not interfere with the optic nerves or chiasm and do not cause visual disturbances. They are found mainly in acromegaly.

3) In the third category are the intracranial-sellar tumors, the most frequent we have to deal with. They grow in both directions, expand the sella towards the sphenoid and grow into the cranial cavity, interfering with the optic pathways. They are recognized in x-ray by an enlarged sella, by changes of the entrance of the sella and by characteristic visual disturbances. These tumors can be solid or cystic, benign or clinically malignant due to their unlimited growth. Only the segment of an intracranial-sellar tumor which is within the enlarged sella is accessible and can be removed.

If we can not remove the whole tumor by the transsphenoidal method, should we look for another operative method which can achieve this goal? My answer is: there does not exist an operative method which can remove an intracranial sellar tumor in its entirety without endangering the patient's life. Exceptions exist. What we can achieve by the transsphenoidal operation is to relieve the optic pathways of their strangulation by the circle of Willis,[7] to promote their recovery and by that the improvement of vision. If nothing else is done the tumor remnant will grow again. Having experienced such incidents in the first patients upon whom I operated, I applied

radium to the surface of the tumor remnant.[7] It took nearly ten years before I found a satisfactory method of application of radium to the surface of the tumor and the adequate dosage.

The first operation which I performed was in 1910, the first trial with radium in 1911, and the final method was developed only in 1920. It took another ten years before it was possible for me to gather sufficient data[5,8] on the duration of freedom from symptoms, especially of visual ones, after combined surgical and radium treatment. For the purpose of the following report a patient was considered improved if his vision was restored to normal or if it became better or if further deterioration of his vision was prevented. He was considered not improved if his vision continued to deteriorate after operation.

In 1937 (the end of the pre-antibiotic era) the number of patients who had been operated upon for pituitary tumors and treated postoperatively by radium application was 277.[7]

The case mortality was 5.4 per cent. The follow-up period for the 262 survivors was 19 years.

Of the 262 postoperative survivors 140 were operated upon from 5 to 19 years before the date of the review; 95 of them, i.e., 68 per cent, showed lasting improvement for this period of time.[7]

Concerning 26 patients who lived for from 19½ to 35 years after operation, I succeeded in obtaining information despite the difficulties following World War II. Twenty-one of this group who were operated upon because of visual disturbances showed lasting improvement from 19½ to 35 years.[5]

During the antibiotic era from 1944 to January 1, 1957, I operated upon 75 patients. I lost one patient in connection with the operation.[5]

Of these 75 patients there were 74 postoperative survivors, 12 died within the first four postoperative years of rapid growing tumors, 27 are less than five years after operation and are not considered in computing lasting results. Thirty-five patients are living or lived

over five years, 24 of them with lasting improvement,[5] i.e., 68.6 per cent.

My intention is to stimulate the rhinologists in this interesting field of surgery which borders on several other fields of medicine.

186 COMMONWEALTH AVE.

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LXVII

MEDICAL AND SURGICAL MISADVENTURES

FRANCIS L. LEDERER, M.D.

CHICAGO, ILL.

There is something very personal in the recitation of a misadventure, only to be related *in familia* or *in camera* as it were. Detailed presentation of 36 years of countless otolaryngologic experiences as bear telling, would require recitation of a voluminous literature. Moreover, the medicolegal gremlin strains its knowing ears and eyes for helpful clues to man's inhumanity to man. Advances in photography permit a vivid and realistic review of the sort of misadventures which the otolaryngologist may experience. Selected photographs, schematic drawings and charts enhance a presentation of a rather practical approach to otolaryngology. They reduce to a minimum the necessity of a detailed account of the mishaps and pitfalls which may occur in the practice of otolaryngology.

In accumulating cases from his own experience and those of 34 other distinguished consultants and specialists, Adolphe Abrahams[1] stated the basic philosophy of this type of reporting when he said: "On the one hand it demands almost superhuman courage to select material from his own humiliating experiences, and with the best intentions it is only human nature to develop amblyopia and deafness in respect to one's own deficiencies. On the other hand, the more comfortable method of enumerating the mistakes of others carries with it an unworthy sense of triumphant condemnation as well as the implication of personal infallibility."

In 1956, Arthur H. Douthwaite,[5] in the presentation of the Croonian Lectures stated, "Vanity, which is the most enduring and widespread of human passions, fortifies the mental censor to suppress the memory of our mistakes, thereby leading to a smugness of outlook which is unendearing. It is only by keeping a record of them that they are not lost. We can learn also from the mistakes of others; these

are less difficult to recall." It was apparent to him, as it has been to others, that "self-criticism is far more important than criticism of others, for, although we may learn by their mistakes, to criticize them directly or obliquely in the presence of colleagues or patients is surely the one unforgiveable sin." This followed Matthew Arnold's statement that "criticism is a disinterested endeavor to learn and propagate the best that is known and thought in the world."

PITFALLS IN SPECIALIZATION

In his presentations on "Pitfalls in Medicine," Douthwaite found that "In tracing the causes of failure in our work it soon becomes apparent that the fault lies more with the physician or surgeon than with the patient or the obscurity of his disease." He learned that mistakes, largely due to vagaries of disease rather than to faulty approach by the physician, can be traced as a rule to unusual patterns of symptoms, less often to puzzling physical signs. On the other hand, the enduring value of diagnosis based on symptoms in the face of contradictory instrumental revelations is to be emphasized. It has been said that we should learn from the mistakes of others because none of us lives long enough to make them all ourselves. As Oscar Wilde stressed, "Experience is the name everyone gives to his mistakes."

We all share Douthwaite's belief that mistakes are inherent in the pursuit of a progressive science, and not to admit them spells death to any hope of advancement in learning. They are not, he holds, confined to the inexperienced, for "paradoxically though it may be, experience may hamper a physician in coming to a correct conclusion. He is tripped up, as it were, by the vast impedimenta of his knowledge, whereas his junior may see the goal clearly. Bias, produced by specialized knowledge, may play havoc with the physician's reputation. It disturbs at once the ability to assess the relative importance of all features of the diagnostic problem, which is the hallmark of the sound clinician."

Otolaryngology bears a kinship to each field of medicine. One of the great dangers of modern medicine, however, is overspecialization. Every specialist becomes so obsessed with his own special field that he disregards its relationship to the body as a whole. The oto-

laryngologist is primarily a physician, secondarily he is a specialist. Douthwaite expressed the same basic idea of Harris P. Mosher,[12] who wrote that "The strength of specialism is specialism. Paradoxically, its weakness is also specialism," in holding that "specialization without extensive knowledge of general medical and surgical diagnosis endangers efficiency." What still prevails, in effect, is the expression of Guillaume Dupuytren (1775-1835) that "Diagnosis holds first rank in our science and is the most difficult part of it, without an exact and precise diagnosis theory is always faulty and practice often incorrect."

POTENTIALITIES FOR ERROR

In evaluating the challenging array of signs, symptoms, and symptom-complexes confronting the otolaryngologist — headache, nasal blockage, dizziness, dysphagia, otalgia, hoarseness, aural or nasal discharge, cough, obstructive states of the upper and lower airway, sore throat, epistaxis, tinnitus, hearing loss, disturbances of facial, orbital or neck symmetry—pitfalls, mistakes, transgressions, accidents, and errors of omission and commission are at times either apparent or evident. Although generally speaking none of these signs or symptoms is in itself diagnostic, all of them require careful evaluation for an accurate diagnosis. Through this medium only is it possible to aid recovery, preserve function of a special sense organ, or save a life. How frequently we falter in this achievement was succinctly pointed out by an analysis made of 1000 consecutive autopsies by a Scandinavian group. This analysis revealed 67 completely faulty diagnoses and even a higher number of inaccurate assessments of the morbid processes during life. Douthwaite commented on this observation as an indication of the error-proneness of physicians and surgeons, and of consultant fallibility.

From the very beginning of the interrogation to the culmination of medical and surgical management of the patient, potential mishaps and pitfalls are numerous. Inasmuch as patients seeking the services of the otolaryngologist confront him with symptoms of a varied nature, definitive management entails a matter of well chosen words and carefully selected modalities. Since all of the special senses are situated in the anatomical areas for which we have prime responsibility, there is need to apply the total person concept. It is necessary

also to employ interviewing techniques and instrumental procedures that will reveal the correct diagnosis, if we are to preserve life and function with minimal emotional upheaval and physical trauma.

THE INTERVIEW

The prevention of iatrogenetic states (physician created) may be anticipated if the emotional factors in illness are recognized and treated. These are engendered by what one says or does not say; by what one does or does not do. There are those physicians whose own psychological composition prevents them from being good listeners. It is a fact that they are so troubled themselves that they cannot listen to the problems of others. So preoccupied are they that it amounts to detached listening when their thoughts are not even concerned with the patient. Others, based on hearsay or an isolated experience, may act prejudicially even before the patient is interviewed. Prejudice is said to be a great time saver for it spares one the necessity of getting at the facts.

The thorny and uneven diagnostic path is replete with error-strewn detours. It is sometimes possible for a diagnostic signal to be observed at the moment of the patient's entry into the office. However, as was so aptly expressed by Jacob Mendes DaCosta (1833-1900), "Diagnosis by intuition is a rapid method of reaching a wrong conclusion." In many instances the preliminary interrogation may reveal the fundamental mistake on the part of the interrogator when he displays imperfect handling of the patient due to bad manners, tactlessness, or impatience. Doubt is often dispelled by permitting a patient to tell his complete story, however lengthy, without interruption, disapproval, or moralization. Interviewing is a problem of communication in which listening (the manner of the interrogator), observing (visual appraisal), and eliciting (recognition of signposts) are paramount factors. All of this requires tact and patience to decide between useful information and what has been described as "garrulous imbecility," and recently as the "Baron Munchausen syndrome," named for that legendary character given to fantastic exaggeration. Frustrating and uncooperative as this type of patient may seem in working toward a common goal of diagnosis, lurking somewhere behind this behavioral screen may be that condition requiring recognition and care, and only amenable to therapy if the process is brought

to light at the time of the interview. Some of these patients may be openly hostile and skeptical. At this juncture the physician's own emotional content requires understanding acceptance of the challenge.

No one would disagree with Douthwaite's opinion that "The more experienced physicians devote a greater time to the taking of the history than to the physical examination. Failure to do so leads to more mistakes than any other error of approach. But even this must be guided by experience, which alone allows us to sift the relevant from the irrelevant. Such a process cannot be taught but must be achieved afresh by each succeeding generation." Here it is that the "gefühl symptome," acquired by clinical experience, wherein common sense or "that part of our knowledge for which we have had no formal training" plays the important role. In interpreting the expression, "do not allow your education to interfere with your learning," it should be emphasized that the myopia of riding pet theories or hobbies frequently jeopardizes satisfactory end-results. Risks of failure are encouraged by conclusions based on inadequate case material. At times one becomes "sensitized" to previous experiences, and being guided accordingly, acquires that feeling of "traditional expectation" in assuming that the very next patient and all others are in the same general classification and will respond in a like manner.

THE MANNER OF THE EXAMINER

Recently popularized recommendations to "see your doctor," have a "cancer prevention checkup" and a "periodic examination" point out the likelihood for erroneous decisions in this group. Beware of the patient who has no complaints but just seeks a routine checkup. He may be the very one with organic change. Thirty years ago Francis W. Peabody[13] emphasized the inherent dangers in the care of patients who have "nothing the matter with them." Although his classic on "The Care of the Patient" was delivered to the students of Harvard Medical School, it bears repetitious reading by those of experience. It reminds one that the doldrums of despair which attend the interview of the so-called "E.N.T. essentially negative" or "not remarkable" patient, or the omnipresent headache, tinnitus, or post-nasal drip complaint may be likened to: "the trees which prevent a view of the forest." A very human reaction to such commonplace complaints, according to Douthwaite, is to truncate the history-taking

in despair and to proceed with the examination. Unfortunately, so many diseases present no physical sign in their early stages that diagnosis may well escape us through impatience. These patients are the very ones for which Francis J. Braceland's[2] suggested leading questions such as "Just how concerned are you and what do you (the patient) think it (the symptom or sign) is doing to you?" The story then may begin to unfold.

The emotional aspects of disease have received prominent "billing" in reference to all fields of medicine. There are those physicians who belittle the role played by emotions, or exclude this factor entirely, and others who overemphasize it. One must learn not to exclude a disease on *a priori* grounds of station in life, marital status, "he comes from a good family," or "I knew him as a child; he's always been unstable." There seems to be no sharp delineation between the emotional and physical aspects of the patient. In otolaryngology, the fallacy is established in considering an incidental observation as the cause of an unrelated condition. It is here, too, that an exaggeration of the negligible, or the inability to recognize the limits of the normal, play an important part in the production of positive errors.

The clinician who ascribes the complaints of a patient to an emotional disorder assumes a grave responsibility. Errors in diagnosis in this direction can threaten the patient's life or, at best, deny him the benefit of treatment, which more adequate diagnostic procedures would make available to him. On the other hand, insistence by the clinician of a physical cause, when the primary one is emotional, can prolong the disease and further solidify the patient's objection to psychiatric evaluation. Referal of the patient for a diagnostic psychiatric interview may clarify the issue in both instances, provided the psychiatrist brings to bear the tools of his specialty, and is, according to D. L. Faucet,[7] humble enough to say occasionally, "I don't know."

TECHNIQUE OF EXAMINATION

The technique of examination of the head and neck areas is too well known to require elucidation. However, it is well to point out that pitfalls await those who overwhelm the patient with the entire gamut of tests known to the profession and to the physician, who

examines perfunctorily and settles for one area or one sign of his particular interest. There is the danger of incompleteness, because the diagnosis appears firmly established. There is also great danger in a sudden inspiration, that flash of insight which Douthwaite claims "sweeps away our difficulties and resolves our problems." The visual recognition of disease which is responsible for the majority of snap diagnoses is losing ground as attention becomes focused on the minutiae of the ancillary sciences. This has been termed "specialistic proneness." It involves dwelling upon certain features of personal interest and the undue tendency to presume the importance of some positive discovery or success in management of another case, especially when all else seems "negative." In this manner the diagnostic field is thrown out of focus because the clinician cannot forget his previous success, thus warping his judgment. The overlooking of another condition, perhaps even a more serious one, while being attracted to the less serious one, is hazardous. In such an instance, one may assume that the structural departure from the normal is necessarily the cause of the illness under investigation. Merrily thus begins the physician's chase after false "diagnostic gods" and often the beginning of the patient's iatrogenic shopping tour.

Skill in employing instruments and other God-given gifts is basic to good otolaryngology as it is to other fields of medicine and surgery. The lacking of same, failing to utilize them correctly, or not doing so at all may be calamitous. It is best illustrated by the following "play" on letters and words:

N	S EEING	L AZY
O	K NOWING	A PATHETIC
T	I NTERPRETING	C ARELESS
	L OOKING	K NAVISH
	L ISTENING	

Physical examinations not only require skill; they demand time. The preoccupied, harassed, overworked, discouraged, fatigued otolaryngologist finds the misadventures in direct proportion to such stresses, as well as those created by too little time and too many outside interests. There is an easy way out of the laborious routine in an effort to make short-cuts by subordination of the physician's examination, by the employment of extraclinical methods or labor saving devices,

snap diagnoses, or by the use of pseudodiagnostic terms such as idiopathic, stress reaction, viral, focal infection, circulatory episode, and many others.

Admittedly, there are times when an absolute diagnosis is rapidly and unequivocably obtained by means of some laboratory investigation. The report itself may bias or even distort the clinician's thinking, and in addition, clerical errors may occur. This may not even be the correct report. A laboratory test is not a substitute for clinical examination, or necessarily acceptable as the negation of a clinical opinion. This holds for clinical reports as well, where the blind or unquestioned acceptance of another's authority may encourage misadventure. Since no one should be offended by the scrutiny of his observations, difference of opinion is legitimate.

DIAGNOSTIC ERRORS

A long but partial list of diagnostic mistakes points accusing fingers at unrecorded errors of omission and commission. 1) The ulcer in the tonsillar area antibiotically treated until malignant disease was apparent even to the layman; the ulcer hidden behind the posterior pillar, residing in the larynx, or in the nasopharynx, as the overlooked cause of an earache, for which cerumen was washed out or ear drops prescribed. 2) The "stuffy nose" for which a douche or nose drops were recommended, when actually a neoplasm was the etiological factor; the same cause so frequently underlying a nosebleed previously diagnosed as simple epistaxis. 3) The headache, which so frequently results in a diagnostic and therapeutic merry-go-round for the patient, finally revealed as an osteoma of the frontal sinus. 4) The otic discharge treated as so-called moist eczema of the canal or a benign suppuration of the middle ear, complacently carried along on antibiotic management when close inspection of the tympanic membrane would have revealed an attic perforation associated with cholesteatoma and possible intracranial complications, or even the presence of a hunting ground for countless remedial agents and diagnoses, only to malignant growth. 5) The cough, which is viewed as the favorite discover an intratracheal neoplasm. 6) The discordant or hoarse voice treated with vocal rest and steam inhalations, when an early indirect laryngoscopy might have disclosed the presence of a neoplasm and prevented costly delay in proper assessment of the true state of

affairs; the same applies to the failure to obtain a chest film or a sputum examination in a tuberculous laryngitis. 7) Otalgia, sought for in the ear itself, when the cause was remote to this area, namely, an ulcerating tumor mass in the larynx. 8) The "lump in the neck" which always involves a diagnostic marathon, the primary lesion of a malignant growth often being present in the pharynx, or in the larynx, or in the nasopharynx. 9) A lesion in the nasopharynx which commonly causes eye discomfort of patients; multiple corrections for errors in refraction finally and obviously become manifest at the sign of ocular paralysis (third and sixth) when a neoplasm invades the cranial base and its foramina. 10) The much abused diagnostic tool, globus hystericus, which leads to mortification of both the physician and the patient when it turns out to be postcricoid carcinoma. 11) Facial pain for which no obvious identifying signs can be detected; it is often judged to be in the range between a hysterical manifestation and a neoplasm of the maxillary sinus eventuating in an acoustic neurinoma whose size finally produces blindness; the same type of lesion causing vertigo, often is treated for a gastrointestinal disorder and the internal ear completely ignored.

PRACTICES WHICH CREATE ANXIETY

Too often does the physician assume that all symptoms must be explained on the basis of an organic or structural abnormality. Modern day information via radio, the press, the motion picture and television is producing a generation of disease-oriented people who have all of the classic symptoms; all the physician has to do is to fill in a few gaps, wantonly aided and abetted by a battery of laboratory tests, all very impersonal, to be sure. In themselves these many procedures, conducted under diverse environmental circumstances by personnel not always given to the simple devices of explanation, may arouse anxieties or focus attention on complaints. The patient may be made sicker than he really is, because the dividing line between the emotional and the physical is somewhat uncertain.

There are many other practices which are alarming to the patient in the course of arriving at a diagnosis. The distraught physician's look of concern (which in so many instances has nothing to do with the case) can precipitate in the patient acute anxiety. The physician's look of surprise or concern, to say nothing of the impressive display

of armamentarium, or the silent walk to a dark room, are traumatic, to say the least. It is a serious error to say too much too soon. The naming of a disease or a condition may be fraught with disaster. It creates invalidism and aggravates existing disease. The premature or pontifical utterances that "these things can cause or become — " and then proceed to dole out what has been given the descriptive appellation of the "bouquet of academic American beauties of differential diagnosis," will undoubtedly set in motion irreversible emotional upheavals. "Floundering in the morass of differential diagnosis," states Douthwaite, "to consider at length the diagnostic possibilities, is academically interesting but laudable only if at the end one commits oneself to a firm opinion." Classically apropos at this point was the aphorism of Oliver Wendell Holmes who said, "Keep your doubts to yourself but give the patient the benefit of your experience."

How much and how to tell have been subjects of numerous contributions to the literature. At times one even asks "Whom to tell?" Undoubtedly it all depends upon what needs to be told, and upon the patient's ability to understand. The clinician who creates iatrogenic diseases or neuroses is likely to be over-anxious, over-conscientious, not certain of himself, and inclined to hedge. He dislikes taking responsibility for a categorical reassurance of his patient and may prescribe "just a little x-drug for safety's sake," or for the same reason orders some laboratory procedure. Although he concedes he finds nothing wrong, he adds, "of course, one cannot be absolutely sure." Other professional types consist of the over-cautious physician with a reputation of being an alarmist; or his cheery breezy opposite, regarded by Abrahams[1] as congenitally incapable of ever imagining the existence of a grave disease, for whom a slap on the back and a guffaw is his way of excusing all of his inexperience, his inadequacies, his indecisions, and even his ignorance.

Ignorance on the part of the clinician is always relative. It may be gross (like overlooking cerumen in the ears, an attic perforation, or the presence of obvious tumors or ulcers), moderate (such as not being acquainted with certain symptoms or physical signs), and then there is condonable ignorance (where he lacks acquaintance or experience with comparatively rare syndromes or diseases). It is of interest also to recognize the same prototypes among physicians are manifest in reference to prognosis. Saying too much, too soon; the

manner of telling, the facial expression, and the mien of the interrogator figure importantly.

THERAPEUTIC MISADVENTURES

Too little concern is usually expressed over the routine "come tomorrow" repeat visit to the physician's office. Anxiety and invalidism are perpetuated by this practice, because it focuses attention of the patient on his complaint and has him thinking he is sicker than he really is. The indiscriminate, repetitious and continuous employment of drugs has a similar effect. The use of nose drops is a typical example of a pernicious habit that becomes a crutch or a dependent addiction to which a physician notoriously contributes. Inflation of the eustachian tube, just for the sake of doing something in irreversible disease of the middle or inner ear, is a flagrant violation of the patient's trust and does not comply with rational therapy. Repeated irrigations of the nose and sinuses because the patient demands or encourages them are likewise practices not to be condoned. The patient's self-made diagnoses and his requests for nasal packs or irrigations weakens, rather than strengthens, the patient's confidence in his physician. The writing for a refill of the patient's favorite prescription certainly does little to elevate the standing of the physician and creates that "dependency strain" of Americans who carry conveniently and habitually a pocket atomizer, a nasal inhaler, nose drops, and the not by any means innocuous, antibiotic throat lozenges. The aphorism, "The physician who treats himself has a fool for a patient," significantly applies to a large percentage of our lay population, who can be "sold" anything if presented in an interesting display, or if championed by a popular radio or television star.

Some time ago, a clinician, concerned with the indiscriminate employment of antibiotics, remarked "these bacteria are not going to take this lying down." It has been our feeling that while we have eliminated the "capitalistic" class of organisms in many instances, we have encouraged the "proletariat." This thought is shared by Douthwaite who stated, "Generations of bacteria, hitherto unknown, with ever-increasing resistance to our drugs, are threatening to overwhelm the human race, which at the moment is only one step ahead in ingenuity to thwart the infinite adaptability of the microbial kingdom." Granted that antimicrobials have increased the therapeutic index of

safety, they are no substitute for an incorrect etiologic and clinical diagnosis, lack of familiarity with the course of the disease, failure to evacuate a suppurative focus or to follow a proper surgical technique.

SURGICAL MISADVENTURES

Surgical misadventures are in direct proportion to diagnostic errors, failures in discussing fully with the patient the many facets of the contemplated procedure, and are compounded by the pitfalls provided by incorrect preoperative preparation, the mishaps which may be entailed in local analgesics or general anesthesia, and those involving faulty or improper instrumentarium. Other factors include the surgical technique itself, postoperative mismanagement, the possible calamitous reactions from the administration of blood and blood substitutes, and the many other errors involving misconceptions, misinterpretations, miscomputations, misjudgments, misstatements, misinformation, human frailties, clerical errors, wrong specimens or x-rays, wrong side, and numerous other blunders, some bordering on plain absurdities. Each surgeon can recall and illustrate instances of misadventure. In the majority of these situations, the human equation was paramount; prevention was possible.

It is essential to view all of these possibilities in relation to the concerned situations or surgical procedures. Operations are divided into the following types: 1) *emergency*, such as a tracheotomy, in which time is of essence; 2) *urgent*, for example in hemorrhage when promptness prevails, warding off catastrophe; 3) *necessary*, as for benign growths, less urgent perhaps, but indicated by the presence of a lesion; 4) *elective*, in the presence of a pathologic process, such as a deviated nasal septum, but without certainty that all symptoms will be relieved by its corrective intervention; 5) *doubtful*, when long-standing septal deformities render the indications rather dubious, and 6) *wishful*, i.e., performed on patients who have no objective disease but who present symptoms presumably justifying an operation based on: a) a "hunch" or intuitive feeling, b) pressure by the patient or his family, or c) because of the surgeon's own intolerance of inactivity, which some believe to be the causative factor in many so-called explorations. In the last three types of surgical indications, the personality of the patient assumes a prominent role in the results of the operation. Furthermore, in creating invalidism and aggravating existing disease,

surgical procedures have no peer. The fact that a patient submits willingly to operation does not justify the need for same; it is, in fact, more often evidence against it.

The same techniques of observing and eliciting are of importance in preoperative discussions with the patient. His previous experiences with physicians, drugs, and operations, his attitudes and his expectations are all of significance. The emotional preparation of the patient is important if the surgery to be performed is to prove successful. If the laryngectomized subject has not been prepared for voice deprivation and his immediate problem of swallowing through a feeding tube, if the adenotonsillectomized child has not been apprised of the reasons for and the resultant discomfiture of swallowing, if the otosclerotic has not been readied for the improvement in hearing or even its further deterioration, catastrophic emotional upheavals may follow. Cosmetic surgery of the nose, face and ears at times presents psychiatric hazards because patients often are neurotically motivated. The selection of patients for operations, especially for elective procedures, must take into consideration the expressions of the patient, his motives and his goals. These factors may reveal the patient's emotional content, thus warding off potential psychotics or litigants.

In coping with emergencies, the need for action is in itself a challenge to the thinking and coordinative processes of the otolaryngologist. A thoughtful clinician can convert an emergency procedure into an elective one by means of intubation, aspiration, and supplying blood. It is a source of debate as to whether hemorrhage or obstruction to the airway is the most difficult emergency to combat. The vivid recollection of the more recent experience will be classed as the outstanding one. Quick thinking, dexterity, and an air of equanimity in the face of odds play the leading roles if morbidity is to be minimized and mortality reduced. In these situations one is likely to find the inefficiency of personnel, the poor planning of physical details, and the lack of effectiveness of a system or organization, heretofore thought to be flawless, revealed in all of its stark reality.

BLOOD TRANSFUSION INCIDENTS

Blood transfusions are such a commonplace adjuvant of medical and surgical therapy that an estimated 3,500,000 procedures are per-

formed in the United States each year. The preventable, untoward reactions are of general interest because it has been estimated one death occurs in every 1000 to 3000 blood transfusions. The likely misadventure lies in the donor aspect (hepatitis or syphilis), the laboratory (clerical errors, inaccurate blood-grouping and cross matching, switching of labels or mislabeling of bottles), and finally in the hospital itself (wrong blood administered due to failure to check accurately and blood is warmed and thereby hemolyzed).

There are 20 to 25 blood groups known, in addition to those commonly typed, viz., A-B-O groups and Rh-HR types are only two of those known. Only in exceptional instances is it practical to check for other groups and besides, such typing is available in only a few laboratories with facilities and technicians for special cross matching methods as the conglutination, the antiglobulin and the proteolytic enzyme tests. Cross matching tests must be done routinely by the conglutination and the agglutination methods. Moreover, for recipients who may have been sensitized by previous transfusions or pregnancies, the antiglobulin cross-matching test must be carried out in order to detect incompatibilities with respect to blood factors such as Kell, Duffy, and Kidd.

ANESTHETIC HAZARDS

Anesthesia has left in its wake a long list of recorded and unrecorded deaths. Recently, a Committee of the Association of Anesthetists (of the British Isles) stated, "If the anesthetic or surgical misadventure had not occurred complete recovery would have been highly probable in 46.9 per cent (of anesthetic deaths)." In reference to locally performed procedures, the need for the same principles that govern general anesthesia should prevail. Mishaps develop in the failure to prevent, recognize, and treat the untoward reactions early, and in erroneously substituting topical agents for injectable material. The environment, office or hospital, must have the same resuscitative means and careful observation of the patient, his blood pressure and his pulse available. Patients are frequently over-sedated and the dose of the analgesic agent improperly controlled. Timing, in spreading its use over a longer period, is not observed. The unknown factors in topical anesthesia are concerned with the lack of uniformity in nebularization; the failure to realize the blood level concentration is

increased by absorption of the drugs via the esophagus and stomach. This is true also of applicator techniques in which the cotton swab is saturated with medicated solution.

The general anesthetic problem develops from a number of fundamental failures in the evaluation of the patient. First, there are the failures to appreciate the significance of visceral disease, including coronary disease, incipient cardiac failure, and nutrition in the geriatric patient. Over-sedation in the aged is also an important factor. In such instances, the patient exhibits signs of intoxication and restlessness. Additional medication given to quiet them really then causes unfavorable reactions. Secondly, there is the failure to appreciate the major surgical risk from the standpoint of the disorders of physiologic functions, not so much as to how much tissue is removed but the site and conditions under which it is removed.

Thirdly, the anesthesia frequently is more hazardous than the surgical procedure justifies. Fourthly, the failure to utilize regional anesthesia, when general anesthesia is being used, in order to protect the patient against harmful reflexes (for example, the carotid sinus reflex). The fifth failure concerns postoperative care when the position of the patient, his blood pressure and pulse are not even recorded, if observed at all (tonsil bleeding, for example). The sixth and final area of failure is that concerned with the importance of being prepared for blood loss. The hematocrit and hemoglobin estimation are counted on too importantly, when it tells only the story of what is in a cubic centimeter of blood but not the true picture of the total blood volume.

THE SURGICAL RISK PATIENT

Now that surgery of magnitude can be performed, the history and physical examination loom importantly. The patient about whose physical and emotional state we are adequately forewarned lives; the patient whose medical evaluation and clearance has not been established does so only by the grace of God. It is difficult and perhaps not even valid to supply a statistical analysis of isolated cases which represent mortality and morbidity in the operating room. Max Sadove and his associate, Herbert Natof of the University of Illinois, studied thirty-one reviews comprising 735 of such case reports. The incidence

of pulmonary and cardiac disease in this group runs higher than in the normal surgical group (in 1942 to 1946 over 45 per cent of patients were so classified).

It is the state of the so-called asymptomatic cardiac patient that is frequently ignored. One never knows just when he will become a candidate for an acute cardiac episode. One of the problems in assessing the patient as a potential risk is the fact that clinicians differ as to what factors in a person render him a good risk. One clinician may feel that a history of two previous infarcts places the patient in jeopardy, whereas another reasons that since the patient had no episode in the past year he can undergo surgery. It is significant that the mortality rate for persons in the 50 to 70 years age group has been found to be higher than in persons over 70 years of age. Even the almost moribund patients of the over 70 group did better. Why? The fact that the surgical "team" becomes more cautious undoubtedly accounts for it.

Finally, about the over-publicized cardiac arrest, an entity well described a century ago. Why the sudden apparent upsurge? Patients subjected to operation today would not even have been considered for surgery ten years ago. Major surgical procedures confer upon the patient the privilege of circulatory collapse and/or cardiac arrest. This, however, does not mitigate against the need for adequate preparation. In prevention, the *sine qua non* of success is the maintenance of adequate respiration and circulation.

THE SURGICAL TECHNIQUE

The technique of surgery is based on correct diagnosis, training, skill and experience. Acquisition of this purely by listening, reading or the purchase of instrumentarium is no assurance of success. Appropriately expressed by Frederick Coller, "surgery is not a technique, it is a process of thinking." Nor is avarice or knavishness among the prerequisites. Over ten million surgical procedures are performed in the United States each year. It is estimated that generalists and other nonsurgical specialists perform about four times as many operations as do surgeons. Specialists in surgery are believed to do about half of the number in the latter group. Members of the profession frequently have wondered just how many of the operations were correctly carried out, if at all indicated.

If the fundamentals of anatomy and pathology are observed and common sense and dexterity are employed, surgery promises uneventful recovery in the large majority of patients. Temporal bone, maxillofacial and neck surgery were never more competently taught and performed. Yet their popularization has brought about a toll of complications, less likely encountered by those more qualified. The same may be said of the many other anatomical areas in the surgical domain of the otolaryngologist. Integrity for the surgeon is imperative. It is also not unreasonable to assume that a wholesome regard for people is as important to the surgeon as is his respect for tissues, for as Hippocrates said, "To heal even an eye, one must heal the whole body."

SUMMARY

The otolaryngologist is confronted with the evaluation of a wide variety of challenging signs, symptoms and symptom-complexes. From the beginning of the interrogation to the culmination of the medical or surgical management of the patient, potential mishaps and pitfalls are possible if not imminent. They reside in the manner of the examiner, the methodology of interrogation, and the thoroughness and technique of examination. The incidence of misadventure is in direct proportion to the diagnostic errors, anesthetic hazards, blood transfusion accidents, and the surgical technique. What is said or left unsaid, what is done or not done, are likewise to be taken into account.

The avoidance of misadventure favors otolaryngologists who are prepared by virtue of knowledge, skill and experience. They avoid riding pet theories or hobbies, and substitute thoroughness for the intuitive approaches or short cuts. Likewise to be avoided is error-proneness and consultant fallibility which result from the development of special interests, favored techniques, and the fallacy of not considering the total person. Attributes of patience, understanding and personal integrity are essential if difficulties are to be avoided and iatrogenesis prevented.

Surgery is more than a technique. It demands a knowledge of indications and judgment with reference to the assessment of the patient. Resourcefulness becomes a matter of split-second timing and

common sense response when the urgency of the moment requires. Avoidance of surgical misadventures is accomplished by careful planning and readiness to meet every expected need. Surgical logistics require skill and the detailed preparation and training on the part of all personnel, both medical and paramedical.

The list of areas of misadventure is long and harried. No one is completely immune and yet, the thoughtful listener and observer is less likely to experience errors of omission and commission. To know one's capabilities and limitations is likewise an asset to the clinician as well as to the patient. There must be an awareness that the responsibility goes beyond oneself in the conduct of a given case. In assessing the total person, consideration must be given to other consultative sources who may offer the patient a better opportunity for complete medical and surgical care. The physical environment and the personnel having to do with the many facets of patient care also figure prominently in the development of mishaps. Avoidance is a matter of the knowledge of the possible existence of these pitfalls and learning from the experience of others.

1853 West Polk St.

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Society Proceedings

CHICAGO LARYNGOLOGICAL AND OTOLOGICAL SOCIETY

Meeting of Monday, December 3, 1956

THE PRESIDENT, DR. RAYMOND W. KERWIN, IN THE CHAIR

Possible Value of Fluorine in the Prevention of Deafness from Otosclerosis and Fibrosis

ALFRED LEWY, M.D.

(Abstract)

The addition of fluorine to the drinking water of Chicago south of 39th Street for the purpose of preventing tooth decay brings to the fore again the question of other therapeutic possibilities. This experiment in public health follows may years of investigation by the dental profession, but there is also considerable literature on the pathological effect of fluorine.

The purpose of this paper is to present what I believe to be a promising and justifiable long range experiment in the use of fluorine for the prevention of some forms of deafness and to suggest investigations which may lead to its trial in other fields of medicine.

The influence of fluorine in living bone and fibrous tissue, especially ligaments, has been the subject of considerable investigation for many years. The literature on this subject was summed up by Roholm in 1937, in a monograph based on his study of cryolite workers and miners in Iceland. He has 893 bibliographic references. The dental literature is also much concerned with dental fluorosis resulting from the drinking of water containing fluorine. The effect extends to the dentin as well as to the enamel, hence the use of the term "dental fluorosis" instead of "mottled enamel." It appears that while toxic quantities of fluorine, variously estimated but approximating two parts or more per million in the drinking water, will produce dental fluorosis

in children, there is a great lessening of dental caries in such communities as have fluorine in their drinking water in less than toxic concentrations, say about one part per million, as compared with communities which have no fluorine at all in the water supply. Hodge claimed the reduction, by one-half, of the incidence of new caries in children by the use of water containing one part per million of fluorine, in which concentration it is not toxic. The subject has been considered more recently by Ast.

Investigations of the direct effect of fluorine on bacteria in the mouth by Bibby and Van Kesteren indicate that a high and toxic concentration is necessary for direct bacteriostatic action.

A survey of deafness in the school children of 68 of Illinois' 102 counties, under the supervision of Dr. Walter Theobald, is now available, and there is a report of Dr. Charles F. Deatherage, head of the Division of Dental Health Education of the Illinois State Department of Health, covering 78 localities in 32 counties in the State.

A total of 132,572 children were examined. Those with defective hearing numbered 6,328, an average for the State of 4.7 per cent.

In the counties whose water does not contain fluorine the total number of children examined was 109,869; the number with defective hearing was 5,406; the percentage defective was 4.9.

In four counties near Chicago whose drinking water contains fluorine not to exceed 1.4 parts per million, from which statistics were available, 20,488 children were examined, the number with defective hearing was 574; the percentage defective, 2.8. In Chicago alone 21,200 children were examined, 922 of whom were found defective, a percentage of 4.3. Chicago drinking water comes from Lake Michigan and is fluorine free.

These numbers are sufficient to overcome to a large extent the elements of coincidence and of statistical error. The population of the four counties having fluorine in the drinking water from which statistics were available is varied. DuPage is largely a medium to high grade suburban residential district plus some farming districts; Will County is largely an industrial and mining district and contains the city of Joliet, with over 42,000 inhabitants; Kankakee is an industrial and farming community; Kendall County contains no large cities and is largely a farming district.

One cannot know how many potential otosclerotic or fibrotic ears are in the group. The few pairs of identical twins with a deafness heritage now being studied by Fowler may offer an occasional opportunity for controls; study of blood serum calcium and phosphorus and the effect of the serum of otosclerotic patients on labyrinthine bone (Grahe and Griebel) might be extended to include the effect of fluorine on such bone as well as its effect on the endocrine system, especially the parathyroid glands.

Ast proposed to test the accuracy of the fluorine-caries hypothesis by placing nontoxic doses of sodium fluoride (to equal 0.8 parts per million of fluorine) in the public drinking water of one community. The plan is to be studied ten or twelve years. Localities are to be selected as to exclude variables as far as possible. The chemical composition of the water, past and present, the composition of the population as to size, color, nativity, age, sex and economic status, the geographic and climatic conditions, diet, and other conditions must be considered, and the same person or persons should conduct the investigation. In the same community the investigation could be extended to the question of deafness, and it could be appropriately done by the United States Public Health Service, and otosclerosis committee of the American Otological Society or any other authoritative body with proper facilities.

It is further suggested that internists and orthopedic surgeons may find here a fertile field for investigation of osteoarthritis and other diseases of the bone, beginning with a survey of the incidence of these diseases in localities which have fluorine in their drinking water in not too high concentration.

DISCUSSION

DR. WALTER H. THEOBALD: Tonight Dr. Lewy is again bringing to our attention a subject which has had more controversy and even political feuds throughout our nation than any other public welfare question. Fluoridation is prevention, not mass medication.

It has been pointed out that both osteomalacia and hyperostosis were observed when experimental animals were fed fluorides at relatively high levels of intake, but that at lower levels, osteosclerosis was observed. However, these findings have not been helpful in understanding the nature of fluoride deposition in man.

The fluoride states are Illinois, Oklahoma and Texas, and the low fluoride states, Indiana and New Hampshire, and Washington, D.C. In the town of Kempton, Illinois, where the fluoride content of the water was from 1.2 to 3.0 ppm, no evidence of bony injury was found by radiologic examination in 86 persons ranging in age from 7½ years to 71 years. Nor was there any evidence of damage found in 31 subjects, age range from 18 to 78 years from Bureau, Illinois, with 2.5 ppm fluorine in the water.

The reference Dr. Lewy has made to our survey of deafness in school children is impressive but not convincing, 4.7 per cent defective hearing in fluorine free water localities compared to 2.8 per cent in four counties with 1.4 ppm fluorine drinking water. Whether or not some of these children were potential otosclerotics, we do not know. It might be revealing if this same group of defective hearing people who have now perhaps reached the age of 40, could be reexamined otologically. It could very well throw some light on the subject of nontoxic concentrations of fluorine in the prevention of otosclerosis.

This is the kind of study which requires a generation or more to evaluate fluorine as a therapeutic agent.

DR. SHERMAN L. SHAPIRO: I would like to ask Dr. Theobald how long those people had been exposed to fluorine who had otological changes.

DR. THEOBALD: These children all were in the school years, up to the seventh grade.

DR. SHAPIRO: How much fluorine had they been taking?

DR. THEOBALD: They were in the areas where the water was fluorinated naturally.

Laryngologists' Aid in Mass Disaster

THOMAS C. GALLOWAY, M.D.

(Abstract)

The importance of an open airway in acute suffocative attacks, especially those associated with infections, has been recognized since Galen. More recently it has been realized that tracheotomy may be life-saving in many other conditions, especially traumatic injuries of the larynx, chest, mouth and jaws; cranio-cerebral injury and cerebral

depression; shock; and flame and thermal chemical injury of the respiratory tract.

Anyone who believes the question of mass disaster is only an academic one should read, with a mind conditioned by the picture of ruthlessness in Hungary, of the devastation in Hiroshima by atomic bombs. Yet, that bomb was only a toy compared to the thermonuclear weapons now available.

In Hiroshima 25 per cent of the 225,000 inhabitants died in four months; 33 per cent of those dying did so the first day. Only 60 of 300 physicians could work, some with injuries. Only three out of 45 hospitals were left usable.

The need for laryngological care of vast numbers of few surviving doctors under chaotic conditions led us to devise a simple method to quickly open the airway. Such a tracheostome should be simple, relatively safe, usable by relatively untrained personnel and easily mass-produced from standard equipment. We are certain the instrument may be much improved. We hope it might be of use in civilian disaster or even in isolated acute respiratory emergencies.

Older trocar type tracheostomes usually designed to be inserted through the cricothyroid could be of only temporary use, and in my experience were not of much value. The Japanese had an instrument which consisted of a knife blade, which was retractable, a collapsed thin tracheal dilator which easily followed the blade inward and a dilator followed by a satisfactory tracheal tube. The Sheldon Riviera instrument used in California is said to have given good service. It is expensive, could not be made in quantity easily, and is now produced only in No. 6 size, which limits its use to adults. The fairly large straight needle used would seem to be dangerous in any hands but those of an expert. We heard that it used a slot and guide, but worked out our own ideas before we saw it.

Our apparatus seems complicated, but really is not. A model made by V. Mueller and Company was presented in October before the Academy. It consists of a curved trocar and cannula with a slot widened at the top and in the anterior concave bend. The end of the trocar is sharpened laterally and rounded on the back. This is started at right angles through the trachea with the neck somewhat extended; then the handle is raised as the trachea is entered obliquely. The trocar is then withdrawn. At this point a small vinyl oxygen

tube may be inserted. The cannula can then be withdrawn, the tube sectioned and held by a metal collar. A second in tandem could then be inserted. Temporary relief could thus be given to many patients in a very short time.

For the usual case a No. 12 Bard Parker knife with the curved point ground nearly to the flat is guided along the slot by a bead braised on the back of the tip, into the trachea. It is then inserted half way along the cannula and is pushed with the cannula into the trachea making either one midline or two diagonal incisions. This is then removed and a modified Jackson tube and obturator is inserted. This also may have a guide bead on its posterior face and a rounded blade set sagittally in its tip and projecting several millimeters forward. A slot permits removal of the armed obturator. After this is inserted, the original trocar cannula is withdrawn. If the original knife incision is made with a V tongue insertion is easier. A simple needle type cannula with the curve of a tracheotomy tube and with a cutting edge and slot on the anterior concavity may replace the trocar and cannula.

This device has worked well on the cadaver and on limited use in the live patient. The method is simple, rapid and easy. Bleeding seems to give no trouble, since the fit is snug. If it should occur, it might be easily controlled by strip packing. If this should present a problem, we propose to adapt a taper luer-type tube with springy side walls which might be expanded for pressure by insertion of the inner tube.

After the original tracheotomy tube with cutting trocar is withdrawn, a standard tube has been easily inserted. We hope that can be routinely done, so that only a limited number of tracheotomies would be required.

DISCUSSION

DR. HAROLD C. LUETH: It is most heartening that one of your very distinguished members is doing an important pioneer task in the field of emergency medical care.

If one looks at the whole problem of mass care under conditions of disaster, there are three major things that physicians must do to cope effectively with the task that confronts them. The first is to stop hemorrhage; the second to maintain an open airway; and third to combat shock.

Depending upon the magnitude of the disaster and the circumstances under which men are expected to work, there are certain principles of mass disaster care that are not fully understood by the profession. It is regrettable that there has been a shift from the teaching of emergency medical care to the more definitive and later aspects of treatment. Even at the founding of the American Medical Association there was included among the aims of the organization a bettering of emergency medical care. Somehow through the years we have drawn away from this objective and have delegated emergency care to someone else. With the present state of the world tensions and the increase in technology it is necessary that we again return to this problem. What Dr. Galloway said about nurses being qualified in these fields is true. All of us know this and seem to be reluctant to come to grips with the real problem of knowing and being able to do those things that will save life and limb. After all, it is a part of the medical approach to any problem of disaster, and one that must be included in future teaching and practice. We had better do a little revised thinking about how we can cope with the present situation, that is being faced in a disaster with too many patients and too little help and too few supplies.

With the very ingenious instrument devised by Dr. Galloway, he has taken an important step in the right direction. It will enable many physicians to do a life-saving tracheotomy under conditions of disaster with confidence.

DR. G. HENRY MUNDT: Obviously we are living in a dangerous age. The instrument that Dr. Galloway has devised appears to be a very excellent addition to our armamentariums. Many of us will try our old Life Saver or do a tracheotomy.

Abstracts of Current Articles

EAR

The Sialographic Differentiation of Mikulicz's Disease and Mikulicz's Syndrome.

Rubin, Philip, and *Besse, Byron E., Jr.*: Radiol. 68:4:477-487 (Apr.) 1957.

Sialographic studies were made of 43 patients in which histologic proof of Mikulicz's disease and Mikulicz's syndrome had been obtained. Twenty-nine cases were of the disease and 14 of the syndrome, the latter group including three leukemias, five lymphomas, five sarcoidosis and one tuberculosis.

The main roentgenographic feature in the disease is sialectosis which on the basis of film findings can be divided into four stages: punctate, globular, cavitary and destructive. Line drawings, description of radiographic findings and radiographs illustrate characteristic changes. This disease is self-limiting and has no mortality. Biopsy is essential to establish definite histologic diagnosis. Conservative treatment is indicated.

In Mikulicz's syndrome are included all those apparent symmetrical enlargements of the salivary and lachrymal glands due to the intimate lymph node enlargement. The salivary gland architecture remains intact in the early to moderately advanced phases. Later the gland structure may be displaced laterally by the increasingly enlarging lymphoid tissue.

In the end stages of both the disease and the syndrome, the gland structure is completely replaced or destroyed. Six figures and 55 references are included.

JORSTAD

The Selection of Patients to be Operated for Mobilization of the Stapes.

De Mumbert, A. V.: Bol. Espan. Otorrinolaringol. Broncoesofagol. 8:18-25, 1956.

In suitable cases of conduction deafness, fenestration results in functional recovery. However, mobilization of the stapes should be

carried out only if specifically indicated, i.e., in the early stages of stapediovestibular ankylosis resulting in deafness and frequently associated with atrophy of the cochlea. This condition may be due to: 1) otospongiosis (Siebenmann-Bezold), 2) Escat's tympanosclerosis, 3) postinfectious fibrosis of the tympanum, 4) rheumatic ankylosis of the tympanum. The postinfectious fibrosis includes various exudative processes of the middle ear due to local or hematogenic infections associated with otorrhea and followed by cicatrization. Another contributory cause may be an earlier myringotomy to evacuate exudate. These factors result in fibrous bands which immobilize the chain of ossicles, displace the tympanic membrane and produce ankylosis of the stapes.

The rheumatic type of ankylosis affects the various articulations of the ossicles and follows fibrous degeneration of the elastic fibers of the ligaments. It is a localization of the general rheumatic condition.

All of these factors result in conduction deafness, either bilateral or unilateral.

Unless the eustachian tube is open, in spite of varying degrees of stenosis, little functional improvement can be expected from mobilization of the stapes. To determine whether or not to operate, meticulous exploration of the stapediovestibular articulation and of the integrity of the cochlea and of the patency of the tubes is essential.

In deafness of transmission auditory response to the whispered voice is reduced by at least ten decibels. Auditory acuity is decreased at all frequencies, especially for the "conversational zone" from 500 to 2,000 cycles per second. Fowler's recruitment test is positive only if there is atrophy of the cochlea. Various audiometric tests may be used to determine the degree and nature of the deafness. The permeability of the tubes can be tested by auscultation and exploration with a semirigid probe. The presence of stapediovestibular ankylosis can be established by the centripetal test of Gellé or by Sullivan's audiometric index, which is based upon a comparison of audiograms of bone conduction with the auditory passage open or obstructed, respectively. In cases of ankylosis the two curves coincide, and the auditory index is below twenty decibels.

Functional improvement following intervention can be expected in cases of uncomplicated conduction deafness. If the causal agents are no longer operative, and the eustachian tubes are completely open,

tinnitus is absent, the auditory loss is not more than thirty decibels by air transmission and not above ten decibels by bone conduction at frequencies of 500, 1,000 or 2,000, Gellé's test is positive or inconclusive, and the Sullivan index is approximately 10.

Surgery is indicated and some improvement can be expected even if atrophy of the cochlea is present to a slight extent and tinnitus is intermittent, if the loss occurs mostly in the low frequencies and is not above forty-five decibels for air transmission and twenty decibels for bone conduction, at conversational frequencies.

Surgery is advised but functional results are not guaranteed if the cochlear atrophy is marked and hearing loss is sixty decibels for air transmission and thirty decibels for bone conduction at conversational frequencies.

Intervention is contraindicated and no functional improvement can be expected if the etiologic factors are still active, hearing loss is greater than sixty decibels for air transmission and above thirty decibels for bone conduction at conversational frequencies, and continuous tinnitus indicates dysfunction of the labyrinth. In these cases even a hearing aid is useless. Some relief may be derived from electrocoagulation of the labyrinth, partial section of the VIII nerve or sympathectomy to eliminate tinnitus and vertigo.

The results of operation vary in individual cases, and are affected by environmental factors, especially the amount of extraneous noise to which the patient is exposed in daily life.

HIGBEE

NOSE

Chronic Sinusitis and Antibiotics.

Hounie, P.: An. oto-rino-laringol. Uruguay 26:1-22, 1956.

Twenty-eight cases of subacute or chronic sinusitis are presented in which the treatment consisted in puncture, lavage, and the instillation of various antibiotics into the sinuses. In 21 cases the sinusitis was localized in the maxillary sinus only. In 7 cases pansinusitis was present. In 22 cases the condition originated in the nose while in the remaining 6 it was of dental origin. In 4 cases the process had

been present for a month before treatment, in 9 for two to six months, in 5 for six months to a year, and in the remaining cases for several years. In one instance it was present for 17 years.

In the 15 cases in which bacteriologic tests were made of the pus from the affected sinuses the causative organisms were Bacillus pyocyaneus (8 cases) alone or associated with other organisms. Staphylococcus was cultured in 6 cases, Pneumococcus in 2 cases and Bacillus coli in one case. In the remaining cases micro-organisms of various species were present in combination and in one case cultures and tests were negative. The predominance of B. pyocyaneus in 40 per cent of cases is striking. In 8 cases the sensitivity of the flora to antibiotics was studied in vitro and treatment was administered accordingly. Chloromycetin had the greatest activity in 6 of the 8 cases followed by streptomycin especially against B. pyocyaneus. Penicillin was moderately active in one case and not at all in the remainder. Aureomycin, terramycin, iloticin, acromycin, erythromycin and bacitracin were given with variable degrees of success.

Of the 28 patients, 20 (71.4 per cent) were cured by puncture. In the remaining 8 cases surgery was necessary.

Following diagnostic puncture of the affected maxillary sinus the antrum was irrigated with physiologic saline solution to flush out the purulent accumulations. The antibiotic was then injected directly into the sinus. This procedure was repeated according to the results obtained. In 12 cases four irrigations or less were sufficient, in one case 10 and in another 14 before the condition was cured. In all cases penicillin was given first in concentrations of 100,000 or 200,000 units, in 3 cc of physiologic saline solution. In 17 cases this treatment was curative and no other antibiotic was required. In the other 3 cases in which B. pyocyaneus was the only organism present penicillin was followed by streptomycin in ten doses of 1 gm, and chloromycetin given in three irrigations of either 25 mg or 1 gm each. In some cases the antibiotics were also given by the intramuscular route.

Cure was determined by bacteriologic tests. In 8 cases of pansinusitis of long standing instillations of penicillin, streptomycin, chloromycin and sodium sulfathiazole were used without success and surgery was required. In the 20 cases in which antibiotics were effective, the lesions were localized in the maxillary sinus and had been of short duration. It is difficult to determine whether the cure was due to the antibiotics per se or to simple lavage, inasmuch as good

results were obtained when only penicillin was given, although this agent was found in vitro to be the least effective as regards bactericidal activity.

Sinusitis of dental origin appeared to be more persistent and difficult to cure than that due to nasal infection. However the extent, severity and duration of the lesions were the determining factors, regardless of the origin of the infection. Bacillus pyocyaneus appeared to respond to treatment more readily than did Staphylococcus.

The author concludes that chloromycetin is the most effective antibiotic in these cases and should be employed for the first instillations and subsequently, unless some other drug is found to be more effective.

HIGBEE

LARYNX

Psychic Dysphonias.

García de Dios, E. P.: Acta oto-rino-laringol. Ibero-Amer. 7:358-364, 1956.

The author differentiates between psychogenic dysphonias which are purely hysterical, hysterical with functional disturbances and hysterical with organic lesions.

In the first group, in which the cords are intact and mobile air is expelled through them but aphonia is complete, except that coughing produces sound. In these cases the loss of voice is due to lack of adaptation of the individual to his environment and occupation. This is sometimes observed in religious groups when an individual wishes to leave the cloistered life and psychically withdraws from it by lack of speech. Sexual or marital maladjustment may also occur in which shock due to involvement in a jealous conflict or to suspicion of a husband's unfaithfulness is the cause. In some cases incompatibility in professional and occupational situations is a causative factor. Students about to take oral examinations frequently lose their voices as do speakers, singers, actors and teachers who are maladjusted and discontented in their work. In all these hysterical cases the loss of voice is due to some subconscious factor which results in lack of will to produce vocal sound and is not intentional or simulated. The individual believes that he cannot speak, and therefore he cannot.

In the second group of hysterical aphonias there are no organic lesions of the larynx or cords but functional disturbances such as spasticity or hypotonus exist. In the absence of actual nerve lesions the cords are distended or relaxed. Muscular contraction causes a metallic, hoarse and disagreeable voice if not total aphonia. The underlying cause is generally some physical or psychic trauma or the shock of witnessing an accident, suicide or violent catastrophe. No subconscious inhibition or maladjustment to the environment is involved. In one such case the patient lost his voice following the explosion of a bomb which caused no actual lesion. It was restored after the surgeon pretended to operate on his larynx.

In the third group there may or may not be a subconscious lack of will to speak but actual organic lesions do exist and are manifested by exudation, hyperemia of the mucosa, slight infiltration, membranous inflammation, and sometimes functional disturbances such as anomalies in the mobility of the cords.

In the first group psychotherapy is indicated. Once the cause is determined, it can be removed by suggestion and the voice is restored. In the second group "theatrical" treatment may be effective. A simulated operation is reported to be completely successful. If this procedure fails, one must resort to psychotherapy.

In the third group the underlying organic changes must first be corrected and then psychotherapy may be given.

HIGBEE

Amyloidosis of the Larynx.

Pietra, R.: An. oto-rino-laringol. Uruguay 26:71-85, 1956.

Two cases of this rare condition are cited. The first patient had noted dysphonia for approximately three months. Palpation of the neck revealed no abnormality, but laryngoscopy showed a smooth, reddish, solid tumefaction with granular surface of the left side of the larynx, extending from the anterior commissure to the arytenoid. The mobility of the larynx was not affected but the left vocal cord was involved. Biopsy revealed cylindric-cell, stratified, fringed mucosa. The chorion was densely infiltrated with amorphous eosinophilic masses with peripheral giant-cells. The condition was an extensive degenerative amyloidosis with macrophagic inflammation.

Operation consisted of a horizontal incision on the left side between the hyoid and the thyroid, resection of the prelaryngeal muscles, resection of the upper portion of the thyroid cartilage and of the filbert-shaped tumor which was friable and difficult to remove. The tissues and skin were sutured, leaving a drainage tube in situ. Recovery was complete.

The second patient had noted discomfort and hoarseness without expectoration for several months, and for a month had suffered from dyspnea on exertion and on lying down. Laryngoscopy showed bilateral infiltration below the glottis and two pale round swellings covered with mucosa and obstructing the laryngeal lumen. Biopsy showed it to be an amyloid degenerative process.

The tumors were both deeply adherent. There was considerable bleeding, necessitating electrocoagulation of the operative field. A tracheal cannula was left in the wound which was sutured. The cannula was removed in fifteen days and recovery was complete except for a slight dysphonia due to a synechia in the anterior commissure of the vocal cords.

Amyloidosis is characterized by an accumulation of an abnormal protein substance, amyloid, resembling starch, which stains blue when treated with iodine and sulfuric acid. It is associated with a polysaccharide containing a sulfur radical similar to chondroitin-sulfuric acid. The condition is due to a disturbance of the endogenous protein metabolism. Some authors claim that the reticuloendothelial system plays an etiologic role.

Three types of amyloidosis of the respiratory passages have been distinguished: 1) primary or idiopathic amyloidosis, 2) amyloid degeneration of benign or malignant tumors present in the larynx, 3) laryngeal localization of a generalized pathologic amyloid condition, either primary, or secondary to chronic suppuration and necrosis of the tissues.

Primary amyloidosis affects men four times as frequently as women and usually occurs between 45 and 65 years. The most frequent sites are the ventricular bands of the larynx, the arytenoepiglottic folds and occasionally the vocal cords or epiglottis. The size of the tumor varies. It may consist of a pseudotumor or of an infiltration or both. It must be differentiated from epithelioma surrounded by local areas of amyloid degeneration.

The symptoms are not specific. Dysphonia is the most frequent manifestation. Dyspnea, cough and occasionally hemoptysis may occur. As a rule there is no pain and no involvement of the lymph-nodes. Laryngeal obstruction may necessitate tracheotomy.

Signs of generalized amyloidosis must not be overlooked. As a rule the parenchyma is affected. The liver and spleen may be enlarged with evidence of hepatic insufficiency. Involvement of the kidney results in symptoms of nephrosis such as: anasarca, albuminuria, hyperproteinemia, hypercholesterinemia and inversion of the serum-globulin coefficient. Hyperazotemia and hypertension are rare. Circulatory insufficiency occurs if the heart muscle is involved. Other localizations are the tongue, thyroid gland or skin in which case yellowish patches form resembling xanthelasma.

Staining with Congo red is conclusive in diagnosis. This stain has an affinity for amyloid substance so that the color disappears from the blood serum more rapidly than in normal subjects. If more than 80 per cent of the stain has disappeared an hour after intravenous injection the diagnosis of amyloidosis is positive. However, in albuminuria a false positive reaction may occur, as the stain is excreted in the urine. A negative result does not exclude the possibility of generalized amyloidosis if considerable amounts of the substance are present. Thus biopsy is necessary to confirm the diagnosis.

The condition develops slowly over several years and does not regress spontaneously. However, the prognosis is favorable. Following complete surgical removal the tumor does not recur.

Amyloidosis must be differentiated from benign polyps of the larynx, laryngocele and malignant tumors. Cancer is distinguished by ulceration, immobilization of the larynx and lymphatic involvement. Amyloidosis is occasionally mistaken for chronic hypertrophic laryngitis, tuberculosis, syphilis, or scleroma.

Surgical extirpation is sometimes followed by galvanocautery or electrocoagulation. The efficacy of radiotherapy is doubtful. Treatment with vitamin E and cortisone has been suggested. In one case 100 mg of ACTH were given daily for fourteen days with excellent results. The effect of cortisone is variable.

HIGBEE

Paralysis of the Abductor Muscles of the Larynx, and Its Surgical Treatment, Resulting in Recovery in Two Cases.

Leguisamo, J. M. A.: An. oto-rino-laringol. Uruguay 26:23-31, 1956.

In a case of nodular goiter subtotal thyroidectomy was followed by severe and persistent dyspnea and suffocation necessitating emergency tracheotomy. Laryngoscopy revealed paralysis of the abductors of both vocal cords without atrophy. Fixation of the cord and arytenoidectomy by the external route (Woodman technique) resulted in full recovery, except for weakness of the voice.

In a second case, treatment with Lugol's solution and bilateral subtotal thyroidectomy to correct goiter and hyperthyroidism had been ineffective. Histologic examination revealed adenocarcinoma which was removed radically. The following year an attack of dyspnea and asphyxia with forced inspiration necessitated emergency tracheotomy. The same surgical technique was employed as in the preceding case and resulted in recovery, except for a postoperative hematoma and ecchymosis. After six weeks the laryngeal cannula was removed, and the patient was able to breathe normally.

In a third case of bilateral paralysis of the abductors following thyroidectomy one of the cords was partially mobile, and respiration was not dangerously impaired. No operation was performed.

This syndrome is of peripheral origin and is always traumatic due to damage to the recurrent nerve during thyroidectomy. The respiratory paralysis is due to closure of the glottis by involvement of the dilator muscles while the constrictors are not affected. The cords are normal in thickness and color and the vibrations are usually unaffected. As a rule, dyspnea, stridor and suffocation appear suddenly, immediately after operation and are so severe as to necessitate tracheotomy.

In some cases as cited above the paralysis is partial and respiration is only somewhat impaired due to anomalies in the branching of the recurrent nerve at a point more distant from the site of the thyroid operation than is usually the case so that the entire nerve is not subject to trauma.

Various methods have been employed to treat the syndrome: 1) restoration of the severed nerve by immediate end-to-end suture or implantation of a nerve into the paralyzed muscles which is rarely

effective; 2) section of the superior laryngeal nerves paralyzing the cricothyroid muscle or section of the upper insertion of the muscle to relax the cords are not effective; 3) tracheotomy is only temporarily helpful in that it assures adequate respiration. The insertion of a cannula with valves is dangerous and useless. Prolonged intubation and dilation of the larynx are of only transitory value and are not recommended; 4) cordotomy by direct laryngoscopy, with section of one or more cords, galvanocautery or cordectomy with fixation of the cords to the walls by laryngofissure do not afford reliable results.

All of these intralaryngeal procedures have the disadvantage that they unnecessarily alter the cartilaginous defense structure of the larynx, damage the mucosa, induce bleeding, favor formation of granulations and involve the anterior insertion of the cords.

Extralaryngeal methods avoid these disadvantages and leave the laryngeal structure intact, the only drawback being some change in the voice.

HIGBEE

Tracheal and Laryngotracheal Stenosis.

Minetti, R. D.: Bol. Espan. Otorrinolaringol. Broncoesofagol. 8:1:5-24, 1956.

On insufficient examination, tracheal or laryngotracheal stenosis may be wrongly diagnosed as asthma, on the basis of the symptoms of fatigue, cough or pain.

Tracheal stenosis may affect the upper, median or lower segment of the trachea, and may be extrinsic, intrinsic, due to abnormalities of the trachea itself, or to foreign bodies. Extrinsic causes include thyroiditis due to infection, cancer of the thyroid gland, or goiter. The latter condition not only compresses the trachea but also results in softening of the walls or lateral displacement of the passage. Tumors of the mediastinum, esophagus, or tracheobronchial adenitis also result in stenosis of the lower tracheal segment. Aortic aneurysm may affect the trachea and is recognized by recurrent paralysis associated with Oliver's sign which is rhythmic pulsation of the larynx corresponding to cardiac contractions. Stenosis may also result from tumors or hypertrophy of the thymus gland.

Intrinsic stenosis is due to inflammatory, traumatic postoperative or congenital conditions of the trachea. The inflammatory causes

include edema, perichondritis, abscesses resulting in cicatricial retraction, chronic lesions due to leprosy, scleroma, tuberculosis and syphilis. The most pronounced symptoms are dyspnea and cough due to compression, hoarseness, substernal pain on swallowing and râles, especially on expiration. The cough is associated with expectoration of fetid, mucopurulent material containing necrotic fragments of tracheal cartilage. In extreme cases the blood vessels near the trachea may be perforated resulting in fatal hemorrhage. Esophagotracheal fistula is another complication.

Cicatricial stenosis may be relieved by metal bougies, bronchoscopes or tracheal cannulas. Recent scar tissue can be removed by curettage or with forceps. However, tough postsyphilitic or scleromatous scar tissue requires incision or mechanical removal by the introduction of a tracheoscopic tube with a mandril attachment, followed by the insertion of short dilator tubes.

Secondary tracheal tuberculosis may be ulcerous, neoplastic or fistulous. Dyspnea is a dominant symptom, and may be paroxysmal and fatal.

Benign tumors of the trachea include pedicled fibroma, lipoma, chondroma, osteoma, adenoma, angioma, papilloma, aberrant goiter, tracheocele and enchondroma. Papilloma is the most common form. Malignant tumors are rare in this location. Epithelioma is the most common form, sarcoma less frequent. Epithelioma occurs most frequently in males than in females. Sarcoma is most common in young individuals.

The first symptom of tracheal tumor is dyspnea, sometimes accompanied by stridor, paroxysmal cough resembling that of pertussis and mucopurulent expectoration. Treatment may be surgery, radium therapy or deep radiotherapy, according to the type of tumor.

Traumatic stenosis may result from lesions due to burns, war injuries, foreign bodies and other factors causing cicatricial contractions. Postoperative stenosis is due less to the trauma of intubation than to prolonged pressure of the tube when the patient is lying down. Laryngotomy sometimes causes articular ankylosis, ulceration and cicatricial malformations.

Congenital stenosis of the trachea is rare. It is sometimes corrected by dilatation with bougies or tubes or by low tracheotomy.

However, in some cases, treatment is unsuccessful and death by asphyxiation occurs.

In all cases of tracheal and laryngeal stenosis, early and complete examination of the respiratory passages is essential, to determine the cause of the condition. Treatment must depend upon the type of lesion.

HIGBEE

Recent Concepts in the Treatment of Laryngeal Croup.

Vassalo De Mumbert, A.: Bol. Espan. Otorrinolaringol. Broncoesofagol. 8:1:25-29, 1956.

Although diphtherial croup is becoming less common, the incidence of croup due to other infections, such as typhoid fever, purulent meningitis, pulmonary or meningeal tuberculosis, tetanus, measles and varicella, is increasing alarmingly. Asphyxia is usually associated with symptoms typical of malignant hypertoxic diphtheria, i.e., extreme prostration, peripheral circulatory insufficiency, oliguria, high fever, and neuroparalytic disturbances.

Laryngoscopic exploration is essential to detect the membranes and exudates which may extend as far as the subglottic region. Secretions should be obtained for cytobacteriologic examination. In diphtherial cases drastic treatment with specific serum (intramuscular doses of 50,000 to 100,000 units) should be followed by antibiotics, preferably penicillin and tetracillin. Laryngoscopic examination should be repeated at intervals of twelve to twenty-four hours and exudates aspirated. If necessary, oxygen and antihistamines may be given. In some cases, strychnine has been given in increasing doses beginning with 0.25 mg. Tracheotomy or intubation may be necessary if the exudates form plugs which obstruct the laryngotracheal lumen, or if there is edema of the mucosa. Tracheotomy is a safe surgical procedure to remove obstructive exudates and membranes, and to ensure normal respiration and afford rest of the affected organ. It is a valuable supplemental treatment in cases of tetanus, poliomyelitis and severe head injuries.

On the other hand, intubation has the drawback that the movements of swallowing, coughing and the patient's change of position increase the irritability of the respiratory passages and may lead to

subsequent stenosis. Intubation does not permit aspiration of exudates.

The antidiphtherial serum antibiotic medication and the aspiration are continued postoperatively.

HIGBEE

MISCELLANEOUS

Modification of the Cicatrization Process Following Tonsillectomy by the Local Application of Penicillin.

Verdaguer, J. S.: Bol. Espan. Otorrinolaringol. Broncoesofagol. 8:1:31-32, 1956.

Tonsillectomy frequently results in large scars, edema, and inflammation of the tonsillar cavity. Painting of the operative site with various substances such as oxygenated water, methylene blue, zinc chloride, sulfamide powder, or powdered penicillin and streptomycin, has given variable results.

Verdaguer used hyaluronidase anesthesia combined with 10 cc of a solution of 200,000 units of penicillin and 0.5 gr of dihydrostreptomycin in 20 cc isotonic serum. He found that the postoperative pain was greatly reduced by this form of anesthesia and that the tonsillar fossae were in excellent condition. A fine layer of membrane formed which gave place to normal granulation scar tissue after three or four days.

HIGBEE

A Panorama of Contemporary Otorhinolaryngology.

Nuñez, G.: Acta oto-rino-laringol. Ibero-Amer. 7:337-351, 1956.

Audiology, audiometry and microsurgery have made great advances in recent years, especially in the diagnosis and indications for surgery in otosclerosis, for mobilization of the stapes, plastic repair of the tympanum and surgical removal of cancer of the larynx. Modern methods of anesthesia and surgery have removed much of the danger of laryngectomy. The electronic microscope is of great value in the diagnosis of cancer. Cancerigenic factors such as tobacco, tar products, hormones and cholesterol are recognized. Some authors attribute

cancer to an ultra-virus and others cite endogenous factors such as embryonic cell displacement or anomalies of the trophoblasts.

Cancer of the larynx and lung are diagnosed more frequently than ever before. This may be due largely to the fact that more cases are recognized by improved methods of exploration and to the tendency of patients to come for examination at the first suspicious sign.

The noxious influence of the release into the air of minute particles of carbon and tar is being investigated also. However, cancer also affects rural inhabitants who breathe fresh air. Furthermore, cancer is not necessarily a condition of the aged but appears in very young individuals as well. Thus age itself is not a causative factor. The conclusion is reached that cancer formation is a matter of environment as well as of any specific agent. Familial predisposition has been noted and it has been found that some individuals tend to develop metastases more readily than do others.

The recognition and localization of subglottic cancer is aided by modern methods of radiography and tomography, by injection of radio opaque material and biopsy. Unfortunately the genesis of cancer is not known. Radiotherapy and surgery are frequently combined, with good results and with a minimum of mutilation. By modern methods it is possible to eliminate the use of the feeding tube which acts as an irritating foreign body. The general and nutritional condition of the patient is greatly improved in consequence.

Most laryngeal tumors, whether in early or advanced stages, should be extirpated. Laryngeal function can be partially restored by re-education.

Radioactive iodine has been effectively used in treatment, and other radioactive isotopes are used in studying the biochemistry of the cancerous tissue and the metabolic changes involved.

In studying the physiology of the nose and disease processes such as catarrh and allergic rhinitis, important results have been obtained by the observation of the nasal cilia in vitro. The mucosal defenses, lysozymes, the pH of the nasal secretion, vascular, lymphatic and nervous reactions have been studied. Ralston and Kerr found relationships between the temperature of the skin and catarrhal and allergic

conditions, and Wolf observed the effects of emotional factors upon the nasal mucosa such as hyperemia, tumefactions of the erectile tissue, and increase in nasal secretion, obstruction and pain extending into the orbit and maxilla. Recent use of adrenocorticotropic hormone (ACTH) and cortisone in rhinology has illustrated the importance of endocrine factors.

Bronchitis, urticaria, headache, hepatic symptoms, persistent or intermittent coryza are now recognized as allergic in origin. Sensitization of the pharynx and larynx by industrial chemicals predisposes to otorhinolaryngologic conditions. Allergic factors may be responsible for some aural syndromes such as tinnitus, Ménière's syndrome and for certain cases of angioneurotic edema. However, of 200 children who underwent tonsillectomy or adenoidectomy, only 13 per cent showed allergic manifestations. Deaths attributed to pressure of the thymus upon the vagus or laryngeal nerves may have been due to anaphylactic shock. Allergy in relation to deafness has been extensively studied. Sinus surgery is often unsuccessful unless desensitizing treatment is given in conjunction.

HIGBEE

Collateral Circulation of the External Carotid Artery and the Internal Carotid Artery Through the Opthalmic Artery in Cases of Internal Artery Thrombosis.

Lin, Paul M., and Scott, Michael: Radiol. 63:5:755-761 (Nov.) 1955.

The authors present studies of five cases of internal carotid artery occlusion in which a definite diagnosis was established by angiographic demonstration of anastomosis of the external carotid artery and the internal carotid artery above the site of occlusion, through the retrograde circulation in the opthalmic artery of the same side. Twelve angiograms to demonstrate these findings are presented. Various factors that can influence the failure of the contrast media to fill the vessel and thus lead to error of interpretation are discussed. Surgical exploration of the carotid artery in the neck may be necessary to determine a definite diagnosis of occlusion. Nine references are cited.

JORSTAD.

Laminagraphy in Acute Maxillofacial Injuries

McClure, Richard F.: Radiol. 65:3:408-411 (Sept.) 1955.

Laminagraphy as the initial radiographic procedure in injuries of the face and jaw has definite advantages: a) positioning of the

head is simple; b) it is unnecessary to repeat the film because of unsatisfactory position; c) laminagraphs often give more information than routine films; d) the ease and accuracy of laminagraphy save time. One weak point is that the malar bone cannot be demonstrated clearly. The technique is described.

Eight laminagraphs of various fractures of the facial bones and mandible are included. There are no references given.

JORSTAD.

Stomatitis From Allergy to Acrylic Denture. Report of a Case.

Tuft, Louis, and Santor, Frank: J. of Allergy 27:261-265 (May) 1956.

Tuft and Santor call attention to the irritating effects of plastic dentures. The ones in common use usually are prepared by mixing the liquid monomer of acrylic resin, called methyl methacrylate, with the powdered polymer, designated polymethyl methacrylate. The mixture then is heated until further polymerization occurs. After subsequent hardening, the familiar pink-colored denture is formed. If the denture is improperly "cured," the presence of the monomer even in small amounts may cause irritation or sensitization. The authors cite the case of a woman who complained of swollen gums with burning and tingling sensations of the tongue which were noted soon after inserting an artificial denture. The authors used some of the liquid monomer, methyl methacrylate, for patch testing. This was left in contact for 48 hours and a positive test was noted. Another time a direct pressure test with the plate was done and a positive reaction consisting of red lines at the points of contact was revealed after 12 hours. This is not in itself regarded as diagnostic and may be nonspecific. Their patient, however, had a positive patch test to the monomer which is indicative of true allergic sensitization and this was substantiated clinically by the fact that she could wear a vulcan denture without any difficulty. The condition is of rare occurrence and is more apt to be found in individuals who demonstrate other manifestations of allergy.

VAN ALYEA.

Books Received

Diseases of the External Ear

By Ben H. Senturia, M.D., Associate Professor of Clinical Otolaryngology, Washington University School of Medicine; with the assistance of Carl F. Gessert, Ph.D., Morris D. Marcus, M.D., Bernard C. Adler, M.D., Fritz M. Liebman, M.D., Lawrence H. Sophian, M.D., Charles D. Carr, M.T., Elizabeth S. Baumann, A.B. Cloth, large 8vo., xiii - 211 pp., many illustrations, 2 color plates, Charles C. Thomas, Publisher, Springfield, Ill., 1957 (Price $8.50).

This is the kind of textbook we like: concise, compact and complete.

In form it is essentially an elaborated outline, the heads and subheads adding greatly to the facility of ready reference; and since the subject is hardly one for continuous cover-to-cover reading this format is very useful.

This work does not share the failing of many contemporary short texts, namely, incompleteness. Too often such books are little more than a re-writing of other such books and are so elementary as to satisfy only an undergraduate. Not so here. All the minute details have had the attention of the authors whose personal studies and contributions are amply reflected in their writing.

Illustrations are plentiful and first rate; documentation is more than adequate and the index—that hall-mark of a good textbook—is all that it should be.

Basic Otolaryngology

By Francis L. Lederer, M.D., Head of the Department of Otolaryngology, University of Illinois College of Medicine, Chief of the Otolaryngological Service, and Abraham R. Hollender, M.D., Professor of Otolaryngology, Emeritus, University of Illinois College of Medicine. Cloth, 8vo., xi - 442 pp., 208 illustrations, 11 large color plates, F. A. Davis Company, Philadelphia, 1956 (Price $6.75).

In text, style and format this book suggests a condensed version of the senior author's previous text books. As in those other works the material is compact and authentic and the illustrations are clear and well-selected. This book should be especially useful to the undergraduate, and will later serve him well as a reference work in general practice.

Magnetic Removal of Foreign Bodies

By Murdock Equen, M.D., F.A.C.S., Chief of Staff, Ponce de Leon Infirmary, Atlanta, Georgia. Cloth, 8vo., 94 pp., 119 illustrations, Charles C. Thomas, Springfield, Ill., 1957.

Environment and the Deaf Child

By Steven Getz, Ph.D., School Clinical Psychologist-Audiologist, California School for the Deaf, Berkeley, California. Cloth, 8vo., xvi - 173 pp., not illustrated, Charles C. Thomas, Springfield, 1956 (Second Edition).

A detailed study by an experienced observer of the best approaches to the problems of the deaf child, based on such factors as age, social maturity, ability to communicate, reading and vocational achievement, sight and intelligence. Fully documented. A large portion of the text is devoted to excerpts from the work of others.

Guide to Medical Writing

By Henry A. Davidson, M.D., Editor of the Journal of the Medical Society of New Jersey. Cloth, 8vo., v - 338 pp., 11 illustrations, The Ronald Press Company, New York, 1957 (Price $5.00).

A handy volume packed full of most things a medical writer should know, from the germination of the idea to the choice of a journal. Most medical authors are only occasional writers, and amateurs in the sense that they do not, at least directly, write for a living. The gap between their inexperience and the printed page which must turn up looking and reading as though fashioned by old and expert hands is the cause of much delay and unnecessary work for everybody concerned. This text is not the usual sermon by the editor-mentor to the author-culprit but shows a fine understanding of the aims and viewpoints of each of them. Recommended to all writers *and many editors.*

Local Analgesia Head and Neck

By Sir Robert Macintosh, D.M., F.R.C.S. (Edin.), F.F.A.R.C.S., M.D. (hon. causa), Buenos Aires and Aix-Marseilles, Nuffield Professor of Anaesthetics, University of Oxford, and Mary Ostlere, M.B., M.R.C.P.E., F.F.A.R.C.S., Research Assistant, Nuffield Department of Anaesthetics, University of Oxford. Cloth, 8vo., 138 pp., 142 illustrations, E. and S. Livingstone Ltd., Edinburgh and London, 1955.

Diseases of the Nose and Throat

By Sir St. Clair Thomson, M.D., F.R.C.P. Lond., F.R.C.S. Eng., LL.D. (Hon.) Winnipeg, Medecin diplome en Suisse. Revised by *V. E. Negus, D.Sc. (Hon.) Manchester, M.S. Lond., F.R.C.S. Eng., F.R.C.S. (Hon.) Edinburgh,* with the assistance of *G. H. Bateman, M.A., B.M., B.Ch. (Oxon.), F.R.C.S. Eng.* Cloth, 8vo., xvi - 1040 pp., 353 illustrations, 46 plates, some in color. Cassell & Co. Ltd., London; Cassell & Co. Ltd., Toronto.

This sixth edition of a universally accepted classic carries out the tradition of the original "St. Clair Thomson" on which most of us were raised, in every respect. The text is comprehensive, authoritative and exact, the illustrations are superb, and as we have noted on a previous occasion in this column, the references are unusually representative and useful. American subscribers are being supplied through the publisher's Toronto branch.

Industrial Deafness, Hearing Testing and Noise Measurement

By Joseph Sataloff, M.D., D.Sc. (Med.), Asst. Prof. of Otology, Jefferson Medical College, etc. Cloth, 8vo., xiv - 333 pp., illustrated. McGraw-Hill Book Company, Inc., New York, 1957 (Price $8.00).

The author of this book enjoys a wide experience in his subject through his association with numerous audiological clinics, with the department of Otology at the United States Naval Hospital in Philadelphia, and as co-director of a special course in industrial deafness for industrial executives, physicians, safety engineers and hygienists conducted at Colby College.

He handles his text under three categories: I. Physical, Physiological, Medical and Medicolegal Aspects; II. Noise Measurement; III. Hearing Testing. A timely and instructive book in a noisy age.

Notices

INDIANA UNIVERSITY

The 43rd Annual Postgraduate Course in Anatomical and Clinical Otolaryngology will be presented by the Indiana University School of Medicine, March 24 to April 5, 1958.

Primarily an intensive course in anatomy of the head and neck, this course includes dissection and devotes 16 hours to the histopathology of otolaryngology. Lectures and demonstrations are designed as a review of basic principles and of recent advances in otolaryngology and bronchoesophagology.

Limited to 24 registrants, the course is open to physicians specializing in ear, nose and throat (eye) and to residents in training in this specialty.

For information address: Division of Postgraduate Medical Education, Indiana University School of Medicine, Indianapolis 7, Indiana.

UNIVERSITY OF MIAMI

The Fourth Postgraduate Course in Esophageal Speech and Organic Voice Problems will be given by the University of Miami School of Medicine, June 16-27, 1958. Specialists in otolaryngology, physical medicine and rehabilitation and speech therapists are eligible. Government grants for training, valued at $250 each, for tuition and traveling expense are available on application. Address: Dr. Homer F. Marsh, Dean, University of Miami School of Medicine, Coral Gables, Florida.

TEMPLE UNIVERSITY
SCHOOL OF MEDICINE AND HOSPITAL

Postgraduate courses in Bronchoesophagology will be given January 13 to 24, 1958, and March 24 to April 4, 1958.

These courses are to be given in the Department of Laryngology and Broncho-Esophagology, Temple University Medical Center, under the direction of Doctors Chevalier L. Jackson and Charles M. Norris.

The tuition fee for each course is $250. Further information and application blanks can be obtained from Dr. Chevalier L. Jackson, 3401 N. Broad Street, Philadelphia 40, Pa.

COLLEGIUM O.R.L.A.S.

The Shambaugh prize, presented every second year by the Collegium Otorhinolaryngologicum Amicitiae Sacrum was recently awarded to Doctor E. Glen Wever of Princeton for his excellent work, over a period of many years, on the physiology of the auditory organ, and especially on the electrophysiology of the ear.

UNIVERSITY OF MANCHESTER

An International Congress on the Educational Treatment of Deafness will be held at the University of Manchester, England, July 15th to 23rd, 1958, with the approval and support of the Council of the University, with financial help from the Ministry of Education, the National College of Teachers of the Deaf, and the Rathbone Trustees, and with the co-operation of the British Council and the Alexander Graham Bell Association for the Deaf, Inc., Washington, D.C., U.S.A.

Forms of application for membership of the Congress will be supplied on request to Professor A. W. G. Ewing, Department of Education of the Deaf, The University, Manchester 13, England.

UNIVERSITY OF MIAMI

Fourth Postgraduate Course in Esophageal Speech and Organic Voice Problems, University of Miami School of Medicine, June 16-27, 1958, under the direction of Nathaniel M. Levin, M.D., F.A.C.S. and Faculty. Specialists in otolaryngology, physical medicine and rehabili-

tation and speech therapists eligible to apply. Government traineeships valued at $250 each (tuition and traveling expense) available on application. Address: Dr. Homer F. Marsh, Dean, University of Miami School of Medicine, Coral Gables, Florida.

UNIVERSITY OF ILLINOIS

The next postgraduate course in Laryngology and Bronchoesophagology to be given by the University of Illinois College of Medicine is scheduled for the period January 27 through February 8, 1958. The course is under the direction of Dr. Paul H. Holinger.

Interested registrants will please write directly to the Department of Otolaryngology, University of Illinois College of Medicine, 1853 West Polk Street, Chicago 12, Illinois.

SET OF BOUND ARCHIVES FOR SALE

There is available for sale a complete set of the Archives of Otolaryngology . . . 64 volumes, from Volume 1, 1925, through Volume 64, 1956; uniformly bound in handsome brown cloth; backbones stamped in gold; in mint condition. For information please address the Editor of the ANNALS, 12 Westmoreland Place, St. Louis.

AMERICAN LARYNGOLOGICAL ASSOCIATION

Copies of the Transactions of the American Laryngological Association are available for general distribution at $8.00 a copy. Please send request with check to:

Dr. Edwin N. Broyles,
Editor Transactions
1100 North Charles St.
Baltimore 1, Md.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION

The American Association for Cleft Palate Rehabilitation will hold its 16th Annual Convention at the St. Francis Hotel in San Francisco on Thursday, Friday and Saturday, April 24, 25 and 26, 1958.

The association is composed of medical, dental and paramedical specialists who are interested in the rehabilitation of persons with cleft lips and palates.

OFFICERS

OF THE

NATIONAL AND INTERNATIONAL OTOLARYNGOLOGICAL SOCIETIES

VI International Congress of Otolaryngology

President: Arthur W. Proetz, M.D., St. Louis, U. S. A.
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President: Dr. Theodor Hünermann, Düsseldorf
Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.

Pan-American Association of Oto-Rhino-Laryngology and Broncho-Esophagology

President: Dr. Jose Gros, Havana
Secretary: Dr. Chevalier L. Jackson, 3401 N. Broad St., Philadelphia 40, Pa.
Meeting: Sixth Panamerican Congress, Brazil, 1958 or 1959

American Academy of Ophthalmology and Otolaryngology

President: Dr. LeRoy A. Schall, Boston
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American Board of Otolaryngology

President: Dr. Gordon D. Hoople, Syracuse, N.Y.
Secretary: Dr. Dean M. Lierle, University Hospital, Iowa City, Iowa

American Broncho-Esophagological Association

President: Dr. Walter Hoover, Boston, Mass.
Secretary: Dr. F. Johnson Putney, 1719 Rittenhouse Sq., Philadelphia 3, Pa.
Meeting: San Francisco, Calif., May 21, 22, 23, 1958

American Laryngological Association

President: Dr. Harry P. Schenck, Philadelphia.
Secretary: Dr. James H. Maxwell, University Hospital, Ann Arbor, Mich.

American Laryngological, Rhinological and Otological Society, Inc.

President: Dr. Percy Ireland, Toronto, Canada.
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Chairman: Gordon D. Hoople, M.D., Syracuse, N.Y.
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American Otological Society

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Secretary-Treasurer: Lawrence R. Boies, M.D., University of Minnesota Hospitals, Minneapolis 14, Minnesota

The American Society of Ophthalmologic and Otolaryngologic Allergy

President: Sam H. Sanders, 1089 Madison Avenue, Memphis 3, Tennessee.
Secretary-Treasurer: Michael H. Barone, M.D., 468 Delaware Avenue, Buffalo 2, New York.

Pacific Coast Oto-Ophthalmological Society

President: H. Leroy Goss, M.D., 620 Cobb Building, Seattle 1, Wash.
Secretary-Treasurer: Homer E. Smith, M.D., 508 East South Temple, Salt Lake City, Utah

The Society of Military Otolaryngologists

President: Captain William C. Livingood, United States Navy (MC)
Secretary-Treasurer: Lt. Colonel Stanley H. Bear, United States Air Force (MC)

Canadian Otolaryngological Society

President: Dr. G.M.T. Hazen, 208 Canada Bldg., Saskatoon, Sask.
Secretary: Dr. G. A. Henry, Medical Arts Bldg., Suite 328, Toronto, Ont.